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A TEXT-BOOK
of
THERAPEUTICS

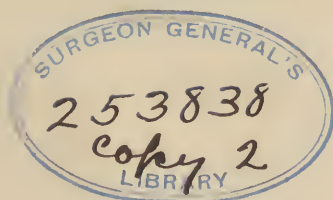
Including the Essentials of
PHARMACOLOGY AND MATERIA MEDICA

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SIXTH EDITION
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PREFACE TO THE SIXTH EDITION

THE advances that have been made in Pharmacology and Applied Therapeutics in the interval between the appearance of the fifth edition of this book and the present one have necessitated many changes in the text. The articles dealing with the most important of the approved remedies have been entirely rewritten, the properties, actions and uses of many new drugs have been considered, the section devoted to Applied Therapeutics has been brought as nearly as possible up to date, and on almost every page numerous minor alterations and additions have been made.

Reference to the following agents appears for the first time: Benzyl benzoate, papaverin, pituitary extract, thyroxin, thromboplastin, methyl alcohol, benzyl alcohol, mercurochrom, germanium dioxid, emetin, yeast, acid sodium phosphate, aluminum chlorid, phenobarbital (luminal), cinchophen (atophan), silver arsphenamin, acriflavin, proflavin, surgical solution of chlorinated soda, chloramins, scarlet red, quinidin, ethyl-hydrocuprein (optichin), surgical paraffin, carbon dioxid snow.

In making the necessary changes, the author has steadily borne in mind the original object of the book, which was to present a concise description of the most important pharmacologic reactions and to show their practical use in influencing the various disturbances that occur in disease.

A. A. STEVENS.

314 S. SIXTEENTH STREET, PHILADELPHIA, PA.
April, 1923

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A TEXT-BOOK OF THERAPEUTICS

GENERAL CONSIDERATIONS

Materia Medica is that branch of medical science which treats of the remedies used in medicine. It deals with their source, physical character, composition, preparations, and doses.

Pharmacy is the art of preparing, compounding, and dispensing medicines.

Pharmacology or **Pharmacodynamics** is the study of the action of drugs upon living organisms. Our knowledge of the action of drugs upon human beings is obtained in two ways: First, by clinical experience, and secondly, by comparative study of their action on the lower animals.

Therapeutics is that branch of medicine which deals with the application of remedies to disease. In its broadest sense, it has to do not only with drugs, but with all other agents which are of service in restoring health, prolonging life, or affording comfort to the sick.

Treatment based solely on clinical experience, and instituted without reference to the pharmacologic action of the remedies employed, constitutes *empirical therapeutics*. Thus, the giving of colchicum in gout and of salicylic acid in acute rheumatism, simply because experience has taught that these drugs often do good, are illustrations of empirical therapeutics.

The treatment of disease by drugs which are expected, from a knowledge of their pharmacologic actions, to antagonize certain known pathologic conditions, constitutes *rational therapeutics*. The employment of chloral in the convulsions of tetanus may be cited as an illustration of rational therapeutics, since it is expected that chloral, through its sedative effect, will counteract the spinal irritation which is manifesting itself in convulsions.

COMPOSITION OF DRUGS

The composition of the organic drugs is often exceedingly complex. They may contain fixed oils, volatile or essential oils,

resins, oleoresins, balsams, gum-resins, enzymes (ferments), alkaloids, neutral principles, toxalbumins (toxins), and organic acids, as well as a variety of compounds having little or no pharmacologic action, such as cellulose, sugar, starch, gum, wax, and coloring matter.

Fixed Oils are compounds of fatty acids and glyceryl, and are obtained chiefly by expression between hot or cold plates. *Fats* differ from oils only in consistence, being solid or semi-solid. Fixed oils and fats are greasy and non-volatile, are insoluble in water and in alcohol (except castor oil and croton oil), but are freely soluble in ether, chloroform and benzin, and when heated undergo decomposition, producing unpleasant acrid vapors. With alkalis they form soaps and glycerin. When fresh most of them are bland and emollient, but on exposure to the air nearly all of them liberate fatty acids, which render them more or less irritant. Those of vegetable origin are obtained chiefly from seeds or fruits, as castor, almond, linseed, olive and cottonseed oils. The chief fats and oils of animal origin employed for medicinal purposes are lard and cod-liver oil.

Volatile or Essential Oils are the oily principles to which many fruits and plants owe their peculiar odor and taste. They are obtained chiefly by distillation. Unlike the fixed oils they are volatile and non-greasy, do not become rancid on exposure, but tend to deteriorate and form resins, do not form soaps with alkalis, and are soluble in alcohol and to a slight extent in water. Chemically, volatile oils consist for the most part either of terpenes or of terpenes and oxygenated aromatic compounds. The terpene or hydrocarbon portion is known as the *eleopten* and the oxygenated portion as the *stearopten*. The latter may be separated from the former by cold or by fractional distillation. Oils of turpentine, copaiba and cubeb are composed chiefly of terpenes, and oils of peppermint, orange, cinnamon, nutmeg, and eucalyptus contain both terpenes and oxygenated products. Camphor, menthol, eucalyptol and methyl salicylate (from oil of wintergreen) are important stearoptens.

Empyreumatic Oils are volatile oils which are not formed in living plants, but are produced either by destructive distillation (oil of tar from pine wood) or by the action of ferments on glucosids in the presence of water (oil of bitter almonds).

Resins are exudations allied to and probably derived from volatile oils. They are oxidized hydrocarbons, amorphous, brittle, insoluble in water, but freely soluble in alcohol. They melt at a low heat, and solidify again on cooling. They unite with alkalis to form soaps. The official resins are rosin (from turpentine), and the resins of jalap, podophyllum, and scammony.

Oleoresins are stable mixtures of a volatile oil and a resin. Their two constituents can be separated by distillation. Important oleoresins are crude turpentine, copaiba, and the oleoresins of cubeb, aspidium, ginger and capsicum.

Balsams are resins or oleoresins containing benzoic or cinnamic acid. The chief balsams are benzoin, storax and those of Peru and Tolu.

Gum-resins are mixtures of resins or oleoresins with a gum. *Gums* are desiccated exudations obtained by incising the limbs and branches of certain plants. They are carbohydrates and are closely related to sugars and starches. They form a mucilage or jelly with water and are insoluble in alcohol. Examples are acacia and tragacanth. Asafetida and gamboge are official gum-resins.

Enzymes or **Ferments** are non-organized compounds which by their mere presence and without undergoing any change themselves produce specific changes in certain other compounds. The enzyme emulsin of the bitter almond in the presence of water splits up the glucosid amygdalin, with which it coexists, into hydrocyanic acid, glucose and benzaldehyd. The volatile oil of mustard is developed from black mustard by the action of the ferment myrosin on the glucosid sinigrin.

Alkaloids are organic compounds of a basic character containing C, H, N, and usually O. Owing to their basic character they readily form salts with acids, and as they do this without liberating hydrogen, they resemble ammonia more than the alkali metals. With the exception of epinephrin from the suprarenal gland, all alkaloids that are used in medicine are of vegetable origin. Alkaloids that are formed by the action of bacteria on animal matter are known as *ptomaines*.

Most of the alkaloids are solids, but a few, such as nicotin, pilocarpin, coniin, and lobelin, are volatile liquids. The salts of the latter, however, are usually solids. Free alkaloids are, as a rule, only slightly soluble in water, but are readily soluble in ether and oils. Alkaloidal salts, on the other hand, are usually freely soluble in water and are insoluble in ether and oils. Both alkaloids and their salts are fairly soluble in alcohol. Alkaloids are precipitated from solutions of their salts in water by many reagents, including alkalis, alkaline carbonates, tannin, iodids, bromids and mercuric chlorid. In many instances, as in the case of strychnin, atropin, morphin, caffenin, and quinin, the alkaloid represents to a great extent the active properties of the crude drug from which it is derived. With alkaloidal salts the acid radical plays an important part in determining the solubility of the compound, although it does not influence pharma-

cologic action; thus strychnin sulphate is much more soluble in water than strychnin hydrochlorid, but the action of the two salts is similar.

In the United States Pharmacopœia all the names of alkaloids end in *ina*, as morphina, cocaina, atropina, etc

Neutral Principles are vegetable principles which have neither an acid nor a basic character but are chemically neutral. The most important members of this group are the glucosids.

Glucosids are bodies which when treated with acids or certain ferments liberate sugar. They differ widely in their solubility in water and alcohol. Examples are the active principles of digitalis (digitoxin, digitalin), of strophanthus (strophanthin), of willow bark (salicin) and of Levant wormseed (santonin). Officially, the names of the glucosids end in *inum*.

Saponins are non-nitrogenous bodies, usually glucosids, which have the property of forming frothy solutions with water, of emulsifying fats, and of dissolving red blood corpuscles. They are found in a number of plants, especially soap bark, senega, and sarsaparilla. They are not absorbed from the intact alimentary canal, but have an intensely irritant local action. When injected intravenously many of them (*sapotoxins*) are extremely poisonous, producing profound weakness and finally fatal asphyxia. After death important changes are found in the mucous membrane of the digestive tract (swelling, congestion and ecchymoses), serous membranes (ecchymoses), and blood (hemolysis).

Toxalbumins or **Toxins** are poisonous proteins of varied origin, some being formed by the microorganisms of disease, as the toxins of tetanus, diphtheria, etc., others being produced by animals, as the venom of poisonous snakes, and others by plants, as ricin of the castor-oil bean and abrin of the jequirity seed. It is characteristic of toxins that when given repeatedly in small doses they lead to the formation of antitoxins, and thus produce a certain degree of specific immunity.

Organic Acids are present in many vegetable drugs, either in the free state or combined with alkaloids or inorganic bases. Important examples are tannic, salicylic, benzoic, acetic, citric, and tartaric acids.

PREPARATIONS OF DRUGS

Vinegars (aceta) are liquid preparations made by treating vegetable drugs with diluted acetic acid. Only one is official—Acetum Scillæ (vinegar of squill).

Waters (aquæ) are aqueous solutions of volatile substances. Among the more important official waters may be mentioned Aqua Ammoniæ (ammonia water), Aqua Cinnamomi (cinnamon

water), Aqua Camphoræ (camphor water), Aqua Menthæ Piperitæ (peppermint water), and Aqua Rosæ (rose water).

Solutions (liquores) are solutions of non-volatile substances in water. Important examples are: Liquor Ammonii Acetatis (solution of ammonium acetate), Liquor Calcis (lime water), Liquor Hydrogenii Dioxidii (solution of hydrogen dioxid), Liquor Formaldehydi (solution of formaldehyd), Liquor Potassii Citratis (solution of potassium citrate), and Liquor Potassii Arsenitis (solution of potassium arsenite).

Decoctions (decocta) are liquid preparations made by boiling vegetable drugs for fifteen minutes in a closely covered vessel, allowing to cool, and then straining. They should be freshly prepared, since they readily decompose. There are no official decoctions.

Infusions (infusa) are liquid preparations made by adding to vegetable substances hot or cold water, allowing the mixture to stand for a certain period, and then straining it. The large dose and the tendency to decompose are disadvantages.

The official infusions are: Infusum Digitalis (infusion of digitalis) and Infusum Sennæ Compositum (compound infusion of senna).

Mixtures (misturæ) are liquid preparations holding in suspension medicinal substances. In some mixtures mucilage or syrup is used to prevent rapid precipitation of the insoluble substance. Mixtures should be well shaken before being administered. The official mixtures are: Mistura Cretæ (chalk mixture) and Mistura Glycyrrhizæ Composita (compound mixture of glycyrrhiza).

Mucilages (mucilagines) are aqueous solutions of gums or other mucilaginous substances. They are used as emollients, as excipients for pills, and for suspending insoluble substances in liquids. The official mucilages are: Mucilago Acaciæ (mucilage of acacia) and Mucilago Tragacanthæ (mucilage of tragacanth).

Syrups (syrupi) are concentrated aqueous solutions of sugar containing medicinal or flavoring agents. Among those in common use may be mentioned: Syrupus Aurantii (syrup of orange), Syrupus Ferri Iodidi (syrup of ferrous iodid), Syrupus Ipecacuanhæ (syrup of ipecac), Syrupus Rhei (syrup of rhubarb), Syrupus Scillæ (syrup of squill) and Syrupus Tolutanus (syrup of Tolu).

Elixirs (elixiria) are sweetened aromatic alcoholic preparations. Two are official: Elixir Aromaticum (aromatic elixir) and Elixir Glycyrrhizæ (elixir of glycyrrhiza).

Spirits (spiritus) are alcoholic solutions of volatile substances or gases. Important examples are: Spiritus Ætheris Nitrosi (spirit

of nitrous ether), Spiritus Ammoniae Aromaticus (aromatic spirit of ammonia), Spiritus Camphoræ (spirit of camphor), Spiritus Chloroformi (spirit of chloroform), Spiritus Glycerylis Nitratis (spirit of glyceryl trinitrate) and Spiritus Menthæ Piperitæ (spirit of peppermint).

Tinctures are alcoholic or hydro-alcoholic solutions of non-volatile (except iodine) substances. They are made by simple solution, maceration, percolation, or maceration and percolation. They are not so strong as the fluid extracts, and, unlike the latter, they are not all of the same definite strength. Most of the tinctures are made with water and alcohol, but some are made with undiluted alcohol. The following are among the most important official tinctures: Tinctura Aconiti (tincture of aconite), Tinctura Belladonnæ Foliorum (tincture of belladonna leaves), Tinctura Cinchonæ Composita (compound tincture of cinchona), Tinctura Colchici Seminis (tincture of colchicum seed), Tinctura Digitalis (tincture of digitalis), Tinctura Ferri Chloridi (tincture of ferric chlorid), Tinctura Gentianæ Composita (compound tincture of gentian), Tinctura Iodi (tincture of iodine), Tinctura Nucis Vomice (tincture of nux vomica), Tinctura Opii (tincture of opium), Tinctura Opii Camphorata (camphorated tincture of opium), Tinctura Strophanthi (tincture of strophanthus), and Tinctura Veratri Viridis (tincture of veratrum viride).

Fluidextracts (fluidextracta) are liquid preparations (alcoholic or hydro-alcoholic) of organic drugs, so made that one mil (one cubic centimeter) represents the active properties of one gram of the crude drug. Important examples are: Fluidextractum Buchu (fluidextract of buchu), Fluidextractum Cascaræ Sagradæ (fluidextract of cascara sagrada), Fluidextractum Ergotæ (fluidextract of ergot), Fluidextractum Nucis Vomice (fluidextract of nux vomica), and Fluidextractum Spigeliæ (fluidextract of spigelia).

Wines (vina) are alcoholic liquids made by fermenting the juice of fresh grapes. *Medicated wines* are alcoholic preparations in which white wine is used as a menstruum. There are no official wines, but Vinum Antimonii (wine of antimony), Vinum Ipecacuanhæ (wine of ipecacuanha), and Vinum Colchici Seminis (wine of colchicum seed) are sometimes prescribed.

Emulsions (emulsa) are aqueous preparations in which, by the aid of some mucilaginous material, insoluble, oily or resinous substances are suspended in the form of minute particles or globules. The chief excipients used for making emulsions are acacia, tragacanth, and yolk of egg. Alcoholic preparations in large quantity are incompatible with emulsions, since they precipitate the excipient, the gum or egg. The official emulsions are:

Emulsum Amygdalæ (emulsion of almond), Emulsum Asafœtidæ (emulsion of asafetida), Emulsum Olei Morrhuæ (emulsion of cod liver oil) and Emulsum Olei Terebinthinæ (Emulsion of oil of turpentine.)

Honeys (mellita) are liquid preparations in which honey is used as a menstruum. The official honeys are: Mel (honey), Mel Depuratum (clarified honey), and Mel Rosæ (honey of rose).

Liniments (linimenta) are liquid preparations containing oleaginous substances, and intended for external application. With the exception of belladonna liniment and lime liniment, which are used as sedative applications, all the official liniments are of a stimulating character, and are to be applied with friction. The official liniments are: Linimentum Ammoniae (ammonia liniment), Linimentum Belladonnæ (belladonna liniment), Linimentum Calcis (lime liniment, carron oil), Linimentum Camphoræ (camphor liniment), Linimentum Chloroformi (chloroform liniment), Linimentum Saponis (soap liniment), Linimentum Saponis Mollis (liniment of soft soap, tincture of green soap), and Linimentum Terebinthinæ (turpentine liniment).

Lotions (lotiones) are weak medicated solutions or mixtures for external use. When intended for the eyes, they are known as *collyria*. Collyria are usually applied by means of a pipet with a rubber bulb. There are no official lotions, but the following are in common use: Lotio Nitra (black wash: $7\frac{1}{2}$ grams of calomel to 1 liter of lime-water), Lotio Flava (yellow wash: 3 parts of mercuric chlorid to 1000 parts of lime-water) and Lotio Opii et Plumbi (lead water and laudanum: lead acetate 4.5 grams; tincture of opium 9 mils; water q. s. ad. 250 mils).

Collodions (collodia) are liquid preparations having for a menstruum a solution of pyroxylin (gun-cotton) in ether and alcohol. They are used externally, and are applied by means of a brush. With the exception of cantharidal collodion, which is used for blistering the skin, they are chiefly employed as protectives. The official collodia are: Collodium (collodion), Collodium Cantharidatum (cantharidal collodion) and Collodium Flexile (flexible collodion).

Glycerites (glycerita) are solutions of drugs in glycerin. The following are official: Glyceritum Acidi Tannici (glycerite of tannic acid), Glyceritum Amyli (glycerite of starch), Glyceritum Boroglycerini (glycerite of boroglycerin), Glyceritum Hydrastis (glycerite of hydrastis), Glyceritum Phenolis (glycerite of phenol, glycerite of carbolic acid).

Enemas or **Clysters** (enemata) are liquid preparations intended for injection into the rectum. There are no official enemas.

Extracts (*extracta*) are solid or semisolid preparations made by evaporating solutions of vegetable drugs. The menstrua are alcohol, diluted alcohol, water, water and ammonia-water, diluted acetic acid, or acetic acid and diluted alcohol. Being concentrated and solid or semisolid, they are well adapted for administering in the form of pills. Among the important official extracts may be mentioned: *Extractum Belladonnæ Foliorum* (extract of belladonna leaves), *Extractum Cascaræ Sagradæ* (extract of cascara sagrada), *Extractum Colocynthis Compositum* (compound extract of colocynth), *Extractum Ergotæ* (extract of ergot), *Extractum Gentianæ* (extract of gentian), *Extractum Hyoscyami* (extract of hyoscyamus), *Extractum Nucis Vomicae* (extract of nux vomica), *Extractum Opii* (extract of opium), *Extractum Physostigmatis* (extract of physostigma), *Extractum Stramonii* (extract of stramonium), *Extractum Sumbul* (extract of sumbul).

Masses (*massæ*) are soft-solid preparations preserved in bulk and intended for forming into pills. The official masses are:

Massa Ferri Carbonatis (mass of ferrous carbonate, Vallet's mass) and *Massa Hydrargyri* (mass of mercury, blue mass, blue pill).

Pills (*pilulæ*) are small rounded masses containing one or more medicinal substances held together by some adhesive material, known as an excipient. The usual excipients are water, glycerin, tragacanth, acacia, honey, bread-crumbs, soap, confection of rose, extract of glycyrrhiza, and extract of gentian. Ordinarily, pills should not exceed in weight 5 grains, unless made of very heavy drugs of small bulk. The official pills are: *Pilulæ Aloes* (pills of aloes) *Pilulæ Asafœtidæ* (pills of asafetida), *Pilulæ Catharticæ Compositæ* (compound cathartic pills), *Pilulæ Ferri Carbonatis* (pills of carbonate of iron; Blaud's pills), *Pilulæ Ferri Iodidi* (pills of ferrous iodid), *Pilulæ Phosphori* (pills of phosphorus), and *Pilulæ Rhei Compositæ* (compound pills of rhubarb).

Confections (*confectiones*) are soft masses made by mixing drugs with sugar and water or honey. There are none official.

Powders (*pulveres*) are drugs in the form of fine, loose, uncompact particles. They are commonly dispensed in small paper packages, known as *chartulæ*. But the latter are not suitable for highly volatile, hygroscopic, efflorescent, or deliquescent substances, or drugs with a disagreeable taste. When not suitable for papers, powders may be dispensed in capsules or cachets. *Capsules* are small gelatin cases or envelopes (hard or soft) in which liquid or solid medicines are enclosed to be swallowed. *Cachets* are round concave wafers made of

flour and water. The drug is contained in the cavity formed by bringing together the concave surfaces of two wafers. Their edges are fastened by being moistened and then pressed together. They are well adapted for enclosing powders having a disagreeable taste. They should be taken floated on a small quantity of water. The official powders are: *Pulvis Aromaticus* (aromatic powder), *Pulvis Cretæ Compositus* (compound chalk powder), *Pulvis Effervescens Compositus* (compound effervescing powder, Seidlitz powder), *Pulvis Glycyrrhizæ Compositus* (compound powder of glycyrrhiza), *Pulvis Ipecacuanhæ et Opii* (powder of ipecac and opium, Dover's powder), *Pulvis Jalapæ Compositus* (compound powder of jalap), and *Pulvis Rhei Compositus* (compound powder of rhubarb).

Triturates (*triturationes*) are fine powders of medicinal substances intimately mixed with sugar of milk. There is only one official triturate:

Trituratio Elaterini (triturate of elaterin).

Tablets (*tabellæ*) are small disks containing medicinal substances mixed with sugar, and pressed into shape by metallic moulds. They are a convenient form in which to administer concentrated remedies, such as calomel, morphin, and strychnin. There are no official tablets.

Troches or **Lozenges** (*trochisci*) are small, cylindrical or flat, solid masses, containing medicinal agents mixed with sugar and mucilage. Most of them are intended to influence the mucous membrane of the throat. The official troches are: *Trochisci Acidi Tannici* (troches of tannic acid), *Trochisci Ammonii Chloridi* (troches of ammonium chlorid), *Trochisci Cubebæ* (troches of cubeb), *Trochisci Potassii Chloratis* (troches of potassium chlorate), and *Trochisci Sodii Bicarbonatis* (troches of sodium bicarbonate).

Suppositories (*suppositoria*) are solid bodies, of various shapes, intended to be inserted into the rectum, vagina, urethra, or nostril. The usual base is oil of theobroma. They are poured while in liquid form into suitable moulds and are solidified by cooling on ice. The only official suppositories are:

Suppositoria Glycerini (suppositories of glycerin).

Ointments (*unguenta*) are soft fatty preparations, melting at the temperature of the body, and containing medicinal substances incorporated with a base of lard, a fixed oil, petrolatum, wax, or spermaceti. The more important official ointments are: *Unguentum Acidi Borici* (ointment of boric acid), *Unguentum Aquæ Rosæ* (ointment of rose-water, cold cream), *Unguentum Belladonnæ* (belladonna ointment), *Unguentum Diachylon* (diachylon ointment), *Unguentum Gallæ* (nutgall ointment),

Unguentum Hydrargyri (mercurial ointment), Unguentum Hydrargyri Dilutum (blue ointment), Unguentum Hydrargyri Nitratis (ointment of mercuric nitrate, citrine ointment), Unguentum Hydrargyri Oxidi Flavi (ointment of yellow mercuric oxid), Unguentum Iodi (iodin ointment), Unguentum Iodoformi (iodoform ointment), Unguentum Phenolis (ointment of phenol, ointment of carbolic acid), Unguentum Picis Liquidæ (tar ointment), Unguentum Stramonii (stramonium ointment), Unguentum Sulphuris (sulphur ointment), Unguentum Zinci Oxidi (ointment of zinc oxid), and Oleates (oleata) are solutions of metallic oxids or of alkaloids in oleic acid. Only one is official: Oleatum Hydrargyri (oleate of mercury).

Cerates (cerata) are solid fatty preparations resembling ointments, but made firmer by the addition of wax. They are of such consistence that they soften but do not melt at the body-temperature. The official cerates are: Ceratum (cerate), Ceratum Cantharidis (cantharides cerate), and Ceratum Resinæ (rosin cerate).

Plasters (emplastra) are solids having a fatty or resinous base, and of such consistence that they do not melt but become adhesive when applied to the surface of the body. The official plasters are: Emplastrum Belladonnæ (belladonna plaster), Emplastrum Cantharidis (cantharides plaster), Emplastrum Capsici (capsicum plaster), Emplastrum Elasticum (rubber plaster), Emplastrum Plumbi (lead plaster, diachylon plaster), and Emplastrum Resinæ (rosin plaster), and Emplastrum Sinapis (mustard plaster).

Poultices (cataplasmata) are soft semiliquid preparations made of some cohesive substance, mixed with water, to be used for applying heat and moisture to the tissues, or for securing a local stimulant effect. They are usually made of flaxseed meal, slippery elm, or bread and milk. Charcoal may be added as an absorbent or mustard as a stimulant. There are no official poultices.

INCOMPATIBILITY IN PRESCRIPTIONS*

Incompatibility in a prescription has been defined as that condition in which there exists either "a chemical decomposition, a pharmaceutic dissociation, or a therapeutic opposition" of its constituents. The term is thus susceptible of three meanings. A prescription is chemically incompatible where chemical change results; it is pharmaceutically incompatible where there is violation of correct pharmaceutic procedure; and there is therapeutic incompatibility where there is antagonism in physiologic action.

* This article has been written by Joseph W. England, PH.G.

Now, accepting these definitions, a prescription may be chemically incompatible, and yet be just what the physician wants. It may be pharmaceutically incompatible, and yet be desirable for the same reason. But it is never desirable when a change of chemical composition or pharmaceutic character results in the formation of new products having totally different therapeutic effects than those obviously intended. And this view—the intended therapeutic action of the prescription—the pharmacist should ever bear in mind.

Every new prescription is largely a law unto itself until tried. Expertness in pharmaceutic manipulation, of which prescription-work is the highest type, is a matter of individual ability, which can be acquired only in the largest and best measures by personal experience. The subject of incompatibility is not a formidable one if there primarily exists a clear knowledge of the chemical or pharmaceutic properties of the substances used, so that any deviation from the right standard may be detected; but here is the puzzling question, How are we to know but that, in the event of some chemical or pharmaceutic change, the physician does not mean just such a change, and nothing else?

At first glance it seems strange, but there are some most successful physicians who, every now and then, write pharmaceutically and chemically, the most incompatible prescriptions. Yet they have success; and their happy results can only be due to the certain formation of new products or an alteration in pharmaceutic character of old ones. It does not follow that all prescriptions thus written are of the highest therapeutic value. Far from it. The tendency of the times is steadily in the direction of greater simplicity in prescription-writing.

It is to be regretted that the physician often depends in large measure upon the pharmacist for detecting any chemical or pharmaceutic incompatibility, and that the pharmacist depends solely and alone upon the physician for recognizing any therapeutic incompatibility. A physician, with his many duties, cannot be expected to have at his command the vast detail of pharmaceutic facts, nor can the pharmacist be considered negligent in not possessing an extended acquaintance with the application of drugs in medicine; but it is clear that some elementary knowledge as to how drugs act and for what purposes they may be employed would be of great practical value to the pharmacist in affording him a clear idea of the therapeutic intent of the prescriber, and the ability to detect any deviation through a chemical or pharmaceutic error. An argument for therapeutic knowledge is not a step in the direction of counter-prescribing. It is only a plea for broader education—for elementary thera-

peutics on distinctly pharmaceutic lines. With therapeutics pure and simple the pharmacist has nothing whatever to do. That is solely the province of the physician. Medicine and pharmacy are making rapid scientific progress—not in the same way, but upon certain definite lines of work and study, yearly becoming more distinct and widely separated, rendering each the more dependent on the other.

To render a knowledge of the solubilities and insolubilities of inorganic compounds readily accessible, the following table is presented, based almost wholly upon Professor Attfeld's "Statement of the Solubilities and Insolubilities of Salts," which expresses, directly or by inference, nearly five hundred soluble and insoluble compounds of the following inorganic basylous radicals: aluminum, ammonium, antimony, barium, bismuth, cadmium, calcium, chromium, cobalt, copper, ferric, ferrous, gold, lead, lithium, magnesium, manganese, mercuric, mercurous, nickel, potassium, silver, sodium, stannic, stannous, strontium, and zinc.

In using this table it is only needful to remember the well-known chemical law that when a solution of a compound is brought in contact with a solution of another compound, and, by an interchange of radicals, an insoluble compound is rendered possible, that compound will be precipitated.

Acetates are soluble.

Arsenates are insoluble, except those of the alkali metals.

Arsenites are insoluble, except those of the alkali metals.

Bromids are soluble, except mercurous and silver; those of antimony and bismuth are decomposed by water to form oxyalts.

Carbonates are insoluble, except those of the alkali metals.

Chlorids are soluble, except those of lead (s),* mercurous, and silver.

Citrates are soluble, except those of manganese, mercurous, silver, and strontium, aluminum (s), barium (s), bismuth (s), cadmium (s), calcium (s), lead (s), zinc (s).

Cyanids are insoluble, except the mercuric and those of the alkaline metals and earths.

Hydrates are insoluble, except those of barium, strontium, calcium (s), lead (s), and the alkali metals.

Iodids are soluble, except those of antimony, bismuth, gold, lead (s), mercuric, mercurous, platinum (s), and silver.

Nitrates are soluble.

Oxalates are insoluble, except those of antimony (s), chromium, ferric (s), ferrous (s), stannic, and the alkali metals.

* (s) means sparingly soluble.

Oxids are insoluble, except those of barium, strontium, calcium (s), and the alkali metals.

Phosphates (ortho) are insoluble, except those of the alkali metals.

Sulphates are soluble, except those of barium, strontium, calcium (s), antimony, lead, mercurous (s), and silver (s).

Sulphids are insoluble, except those of barium, calcium (s), strontium, and the alkali metals.

Sulphites are soluble, except those of aluminum, antimony, barium, bismuth, calcium (s), cobalt (s), copper, ferrous (s), lead, manganese (s), nickel (s), silver, stannous, strontium, and zinc (s).

Tartrates are soluble, except those of antimony, barium, bismuth, cadmium (s), calcium (s), copper (s), ferrous (s), lead, manganese (s), mercuric, mercurous, nickel (s), silver, strontium (s), and zinc (s).

Acids decompose hydrates, carbonates, and acid carbonates to form salts; the stronger acids, which are largely inorganic, set free the weaker acids, which are largely organic; or, brought in contact with alcohol or alcoholic solutions, form ethers; alkaline hydrates, carbonates, and acid carbonates neutralize free acids, decompose some glucosids, and precipitate all alkaloids, some of which precipitates are soluble in excess of the precipitant, or in alcohol, if that liquid be present in sufficient amount to dissolve them.

Oxidizing agents, such as nitric, hydrochloric, nitrohydrochloric, picric, and chromic acids, and potassium bichromate and permanganate, with readily oxidizable substances, such as carbohydrates, alcohols, ethers, sulphur, phosphorus, sulphids, and organic matter in general, form explosive compounds. Potassium permanganate, if ordered in pill form, can best be made with cacao butter and cosmolin in very small quantity, and enclosed in gelatin capsules. Silver nitrate is reduced by organic matter to oxid, with the exception, it is said, of opium and extract of hyoscyamus. A very good way of making pills of it is with cacao butter and cosmolin, etc., as mentioned above under potassium permanganate. Syrup of ferrous iodid and potassium chlorate form a poisonous compound, and potassium iodid and potassium chlorate form a mixture which yields the poisonous iodate on being taken internally.*

Iodin and iodids yield precipitates with the alkaloids; bromids precipitate morphin and strychnin salts on standing, but a few drops of dilute hydrochloric acid added, after the addition of the alkaloid, prevents the change. Sodium biborate precipitates morphin and cocain salts, but on the addition of a

* *Am. Jour. Phar.*, p. 277, 1876.

small quantity of boric acid, or with boric acid alone, precipitation does not take place. Mercuric chlorid with acidulated solutions of the alkaloids forms crystalline double salts; potassium-mercuric iodid precipitates alkaloidal solutions. Solutions of quinin salts with those of the alkaline acetates, or with Basham's mixture, precipitate the sparingly soluble quinin acetate. Morphin solutions give the phenol reaction if mixed with tincture of ferric chlorid.

Glucosids are decomposed by free acids and precipitated by tannin. Tannic and gallic acids precipitate alkaloids, albumin, gelatin, and the majority of metallic salts, and yield inks with iron solutions.

Resinous tinctures and fluid extracts prescribed with aqueous solutions should always be emulsified with acacia; tinctures and fluid extracts made of stronger alcohol, mixed with those made of diluted alcohol, become turbid and precipitate, since the special solvent power of alcohol or of water for a substance diminishes in proportion to the quantity of the other liquid present. A "shake" label should always be used.

When for internal use, fixed and volatile oils and oleoresins with aqueous solutions should always be emulsified, whether ordered or not, and to better emulsify the volatile oils they should have mixed with them, prior to emulsification, an equal volume of olive, almond, or cotton-seed oil.

Tincture of ferric chlorid gelatinizes mucilage of acacia; free acids separate insoluble carminic acids from compound tincture of cardamom; free acids precipitate glycyrrhizin from fluidextract of licorice.

Commercial spirit of nitrous ether liberates iodine from solutions of iodids, decomposes antipyrin solutions to form a green nitroderivative, and precipitates mucilage of acacia, but if it be well diluted with water it can usually be added last without precipitating. Tincture of guaiac and spirit of nitrous ether are stated to be pharmaceutically incompatible by Potter, although they are sometimes prescribed together; likewise infusion of wild cherry with compound infusion of gentian, infusion of cinchona with compound infusion of gentian, and infusions with metallic salts generally.

Sodium salicylate in solution precipitates the sparingly soluble salicylic acid if mixed with acids, and yields, if dispensed in powders with potassium acetate, the very deliquescent potassium salicylate. Sodium salicylate in strong solution is decomposed by tincture of ferric chlorid, but if well diluted first changes into ferric salicylate. Sodium benzoate in solution is decomposed by acids to yield the sparingly soluble benzoic acid.

Mercuric chlorid is decomposed by solution of potassium arsenite, but if the alkaline solution has first added to it, in slight excess, diluted hydrochloric acid, no precipitation will take place on the addition of the mercurial salt. Pyrophosphate and phosphate of iron solutions precipitate with dilute phosphoric acid. The National Formulary recommends the usage of dilute metaphosphoric acid in place of the official "ortho" variety, as yielding a permanently clear solution.

In conclusion, the writer would say that in this brief article he has endeavored to present, not an exhaustive list of special incompatibles, but simply a general expression of those liable to occur in the every-day routine of prescription-work.

METHODS OF ADMINISTERING DRUGS

By the Mouth.—This is the most common method. Drugs may be administered by the mouth for their local action on the mouth, throat, stomach, or intestines, or for the purpose of being absorbed. When it is desired to influence the mouth or throat, the remedy is generally given in the form of a lozenge, and the patient advised not to take food or water for at least an hour afterward. Remedies intended to act directly on the mucous membrane of the stomach should be given when the stomach is empty, that is, half an hour or an hour before meals. Drugs intended to exert a direct influence on the intestine should be given two or three hours after meals, and preferably in firm pills. Sometimes such pills are coated with substances, such as keratin (obtained from horn) and salol, that are more or less resistant to the action of the gastric juice.

Absorption may take place from any part of the alimentary canal. Very volatile remedies, such as the spirit of nitroglycerin, are readily absorbed from the tongue. Absorption from the digestive tract is effected most quickly, as a rule, when the drug is given in solution on an empty stomach. However, in the case of remedies that have an irritant local action, it is much better to give them immediately after meals, so that by becoming mixed with the food their local effects are more or less avoided.

Hypodermic Method.—This consists in injecting medicinal solutions or suspensions into the subcutaneous tissues by means of the hypodermic needle and syringe. The advantages of this method are the rapidity with which absorption is effected and the certainty of securing the action of the entire dose, since partial destruction of the remedy by the digestive organs is avoided. The disadvantages of this method are the pain inflicted, the liability of causing abscess, and the risk of throwing the solution directly into a vein. Many drugs cause less irrita-

tion and are absorbed more rapidly when injected into the substance of the muscles rather than into the subcutaneous tissues. The alkaloidal salts, on account of their small bulk, are especially adapted for hypodermic use. Some remedies, such as toxins and antitoxins, are effective only when administered subcutaneously or intravenously. The best places to select for the injections are the extensor surface of the arm, the calf of the leg, the abdominal wall, and the buttock. Both the needle and the solution should be sterile. All the air should be expelled from the syringe before the injection is given, and care should be exercised to avoid entering a vein. The dose of a drug administered hypodermically is ordinarily about one-half of that given by the mouth.

Intravenous Injection.—This method is employed when a very prompt and powerful effect is necessary, especially if the drug is too irritant to be given hypodermically (sodium bicarbonate in diabetic coma), if the circulation is so feeble that absorption from the subcutaneous tissue is likely to be slow (strophanthin in acute dilatation of the heart), or if the drug is one that loses its potency in passing through the subcutaneous tissues or the wall of the digestive tract (epinephrin). In administering drugs intravenously the patient should be in the recumbent position during and for an hour or two after the injection; a very fine highly polished needle should be used; the needle should be sterilized and the skin prepared as for a surgical operation; the vein (median cephalic) should be engorged by massage of the forearm in a downward direction and the application of an Esmarch bandage or rubber band above the elbow; the needle should be introduced at an acute angle and so slowly that there is no likelihood of piercing the distal wall of the vessel; the bandage should be released after the introduction of the needle into the vein and before the injection is begun; the medicament should be injected slowly, the piston being pushed forward and rotated at the same time; and after the injection the needle should be quickly but gently withdrawn, and the puncture touched with tincture of iodine and sealed with collodion.

Intra-arachnoid Injections.—This method is employed to produce general anesthesia with such drugs as cocaine and stovaine and to bring remedies in direct contact with spinal cord in such diseases as cerebrospinal syphilis, locomotor ataxia, cerebrospinal meningitis, and tetanus.

By the Rectum.—Absorption through the rectum is effected much less rapidly and with less certainty than through the upper bowel. To accomplish the same result it is generally necessary to give twice the dose by the rectum that would be required by the

mouth. This method is convenient when the stomach is unretentive. It also affords a means of acting directly on the bowel with drugs, and of removing hardened feces, flatus, and parasites. When the enema is to be retained in the bowel for its local effect, the fluid should be warm, the quantity should not exceed 2 ounces, and the injection should be made very slowly. When the enema is intended to bring about defecation, 1 or 2 pints of fluid may be employed. When flatus is to be removed, an enema consisting of from 4 to 6 ounces of the emulsion of asafetida is effective. Both local and constitutional effects may also be secured by means of suppositories containing medicinal agents.

Inunction.—Many medicinal substances, if dissolved in fats, are fairly well absorbed through the unbroken skin, especially if friction be used in their application. When this method of administration is employed systematically to secure a constitutional effect, different surfaces should be selected each day. The best surfaces for inunction are those having a thin skin, such as the axillæ, popliteal spaces, the groins, and the inner sides of the thighs. The drugs that are most frequently introduced by inunction are mercury and iodine.

Inhalation.—Volatile drugs are rapidly absorbed from the respiratory tract, and this method is especially employed for the administration of drugs which induce general anesthesia, such as ether, chloroform, and nitrous oxid. The effect of other volatile substances, such as amyl nitrite, is also secured by inhalation. Medicated vapors and sprays are employed to influence directly the mucous membrane of the respiratory tract.

CONDITIONS MODIFYING THE EFFECT OF DRUGS

The effect of a drug is modified by many conditions, the chief of which are dosage, age of the patient, sex, weight, disease, idiosyncrasy, frequency of administration, time of administration, avenue of administration, and association with other drugs.

Dosage.—The effect of a drug varies not only quantitatively with the dose, but also, in some instances, qualitatively. Thus, ipecacuanha in minute doses may have an antiemetic effect, while in large doses it is a powerful emetic.

Age.—Children require smaller doses than adults. Two rules are in common use for determining the proper dose for children of different ages:

Young's rule is as follows: Add 12 to the age and divide by the age, and the quotient will be the denominator of a fraction the numerator of which is 1. Thus, for a child of four years,

$$\frac{4 + 12}{4} = 4, \text{ and the dose is } \frac{1}{4} \text{ that for an adult.}$$

Cowling's rule is to divide the age of the child at its next birthday by 24. Thus, for a child 3 years old, the dose would be $\frac{3}{24} = \frac{1}{8}$ of the adult dose.

These rules, of course, are only approximately correct, and each drug must be considered by itself in reference to dose. Thus, children are very susceptible to opium, and, therefore, the dose of this drug must be smaller than the age would apparently indicate. On the other hand, arsenic and belladonna are well borne by children, and, therefore, relatively larger doses of these drugs may be prescribed.

Sex.—Women generally require smaller doses than men. The dose for a woman is about $\frac{4}{5}$ of that for a man.

Weight.—Many physicians do not consider the weight of the patient in determining the dose of a drug, but it is really an important factor. The effect of age and sex upon dosage is due in large part to difference in weight.

Disease.—Digitalis does not increase the output of urine in healthy persons, but when the urine is scanty owing to failure of the circulation and venous engorgement of the kidneys it is an efficient diuretic. Again, acetanilid does not influence the body temperature in health, but in the presence of fever it has a marked antipyretic effect.

Idiosyncrasy.—This is a condition in which a patient responds in some unusual way to a drug or reacts more readily or less readily to the ordinary dose than is customary. In some individuals a grain of quinin will produce a diffuse erythematous rash. Five grains of antipyrin have not rarely produced symptoms of collapse in susceptible patients.

Frequency of Administration.—In some instances the continuous use of a drug results in increased *tolerance*. This is particularly true of nicotine, alcohol, opium and other narcotics. The acquired relative insusceptibility may depend upon increased destruction of the poison, to increased elimination and diminished absorption, or to a production of antibodies (antitoxins). In many cases, however, it appears to result from a change in the tissues themselves, whereby they are rendered less sensitive to the action of the drug.

Small doses of certain drugs when given repeatedly not rarely produce after a time much more pronounced effects than they did during the early period of their administration. This is known as *cumulative action*. It is probably due in most instances to an accumulation of the drug in the tissues, excretion, for one reason or another, being less rapid than absorption. In some cases, however, it may depend upon irregular absorption, a large quantity of the drug suddenly entering the circulation from

the alimentary canal, where, owing to some accidental condition, there has been an undue accumulation. Cumulative action occurs most frequently with bromids, iodids, mercury, arsenic, digitalis and strychnin.

In the case of foreign proteins (serums) repeated administration is occasionally followed by a very violent reaction (*anaphylaxis*), which is due to increased sensitization of the individual (see p. 464).

Time of Administration.—Saline cathartics act best, as a rule, when taken in the morning on an empty stomach. Somnifacients are most effective when taken in the evening, as then the brain is already fatigued and the patient's surroundings are more tranquil. The effect of acetanilid and other antipyretics is most pronounced in febrile conditions when given about the time of a usual remission of temperature.

Avenue of Administration.—Drugs act much more promptly and powerfully when given intravenously or subcutaneously than when given by the mouth. Indeed, some remedies are only effective when given intravenously or subcutaneously. This is true of the various antitoxic sera and of arsphenamin. Epinephrin influences the circulation only when administered intravenously, although it relaxes the bronchi and often affords relief in asthma when given subcutaneously. When given by the mouth its effects are virtually limited to the mucous membrane of the stomach.

Association with Other Drugs.—The simultaneous administration of two or more drugs having a similar action often produces a more pronounced and agreeable effect than can be secured from the use of one drug alone, even in large dose. Drugs which aid each other in this way are known as *synergists*. Several laxatives given together often yield better results than any one given alone. In insomnia a combination of a bromid with hydrated chloral has advantages in many cases over either drug alone. On the other hand, one drug may completely neutralize the effect of another. Such opposing agents are termed *antagonists*. On the bowel, opium and the vegetable cathartics have an antagonistic action; atropin neutralizes the influence of pilocarpin on the sweat glands; and strychnin opposes the depressing action of bromids on the spinal cord.

DRUGS

CIRCULATORY STIMULANTS

Circulatory stimulants are drugs which increase the efficiency of the heart. The most important members of this class are:

Digitalis
Strophanthus
Squill

Apocynum, convallaria and adonis, although less reliable, have apparently a similar action.

These drugs act directly on the cardiac muscle (1) increasing its tonicity, contractility and excitability; (2) lessen the conductivity of the auriculoventricular bundle; and (3) stimulate the vagus center. In animals large doses administered intravenously also constrict vessels in certain areas by acting directly on the arterial muscle.

The effect of pure vagal stimulation is to prolong the diastolic pause and to render the ventricular contraction less complete. Although the lengthening of the diastole gives the heart a longer resting period and permits of more complete filling of the ventricles, the blood pressure is actually lowered and the output of the heart is decreased, on account of the weakened systolic contractions. However, drugs of the digitalis group improve the pulse volume and increase the output of the ventricles both per beat and per minute, as their pronounced stimulant action on the cardiac muscle much more than offsets the depressing effects of vagal stimulation.

A number of drugs quicken the heart-beat and slightly increase the output of the heart per unit of time, not so much by acting on the heart directly as by causing peripheral irritation and a reflex stimulation of the organ. The effect of these drugs on the circulation is necessarily transitory. The important members of this group, which are often referred to as *diffusible cardiac stimulants*, are:

Ammonia
Alcohol

Ether
Camphor

Four other drugs have some claim to be considered among the circulatory stimulants, namely:

Caffein
Strychnin

Epinephrin
Pituitary Extract (posterior lobe)

The actions of *caffein* on the circulation are more or less antagonistic to one another; nevertheless, the total effect of therapeutic doses, while not constant, is usually to increase slightly both the pulse-rate and the output of the heart per unit of time. Its side-actions, especially those on the cerebrum, detract somewhat from its usefulness as a circulatory stimulant.

Although *strychnin* has no direct effect upon the heart and is but a feeble vasoconstrictor, the weight of clinical evidence is in favor of its usefulness in certain forms of circulatory weakness, especially those in which there is general weakness or depression. It is possible that the good effects of the drug may be due to an improvement of the general vascular tonus brought about by its action on the central nervous system.

Both *epinephrin* and *pituitary extract*, when administered intravenously cause a pronounced, though transitory, elevation of blood pressure; epinephrin causing vasoconstriction by stimulating the sympathetic nerve-endings in the vessel-walls and pituitary extract causing vasoconstriction by stimulating the arterial muscle itself. Both drugs produce a slowing effect upon the heart by raising the blood pressure and thus indirectly stimulating the vagus center in the medulla. Upon the cardiac muscle itself epinephrin has a direct stimulating effect, while pituitary extract apparently exerts a depressing influence.

Increase of Blood Pressure.—A drug may increase the blood pressure (1) by stimulating the heart directly; (2) by constricting the vessels directly (stimulation of arterial muscle itself or of the sympathetic endings in the arterial muscle); or (3) by constricting the vessels through a central action. Blood pressure may be raised also by increasing the amount of fluid in the vessels (intravenous injection of blood or of saline solution) or by compression of the peripheral vessels, as in the pneumatic rubber suit devised by Crile.

Acceleration of the Heart Beat.—This may be brought about (1) by excitement or peripheral irritation (alcohol, ether); (2) by stimulation of the heart itself (caffein); (3) by direct depression of the vagus, centrally or peripherally (atropin); (4) by reduction of blood pressure and indirect depression of the vagus center (nitroglycerin, amyl nitrite); (5) by stimulation of accelerator mechanism of the heart (cocain, partly in this way).

Indications for Using Circulatory Stimulants.—Circulatory stimulants are indicated in heart failure and vasomotor paresis from various causes. In *collapse* quickly acting (diffusible) stimulants, such as ammonia, alcohol and camphor, are

often effective, especially if their administration is associated with the external application of heat and the injection of warm saline solution intravenously, subcutaneously or into the rectum. In *shock* the same measures may also be used, and, in addition, epinephrin or pituitary extract may be given intravenously to constrict the peripheral vessels and thus increase the tonus in the medulla.

Circulatory stimulants of the digitalis group are very useful in *myocardial insufficiency*, especially when this is associated with dilatation of the heart, mitral and tricuspid insufficiency, and evidences of general venous congestion. The good effect of these drugs is due chiefly to their power to improve directly the tone of the cardiac muscle, and, in case of auricular fibrillation, a common accompaniment of chronic myocardial disease, to lessen the conductivity of the auriculo-ventricular bundle, thus protecting the ventricle from the exhausting influence of the multitudinous irregular contractions arising in the auricle. Epinephrin and pituitary extract, owing to their transitory effect and the necessity of administering them intravenously, are of no value, of course, in persistent cardiac failure.

In the *circulatory weakness of the acute infections* the effects of the digitalis group are less certain, although good results are often obtained.

DIGITALIS, U. S. P.

(Foxglove)

Digitalis is the dried leaves of *Digitalis purpurea*, a biennial herb growing in Central and Southern Europe. It contains several principles, all of which are of the nature of glucosids, the most important being *digitoxin*, *digitalin*, *digitalein*, and *digitonin*. The first three produce the characteristic digitalis effects. Digitonin is present only in traces. It is a member of the saponin group and is not absorbed from the digestive tract. It is, however, a local irritant. Digitoxin, the most powerful constituent, is readily soluble in alcohol, but almost insoluble in water; digitalin is readily soluble in alcohol and slightly soluble in water; digitalein is soluble in both alcohol and water. Digitonin is soluble in water, and although it is without the actions the digitalis bodies, it aids as a saponin in bringing the insoluble and most active constituents of digitalis into suspension, as for instance, in the infusion.

PREPARATIONS	DOSE
Tinctura Digitalis, U. S. P.	5-20 min. (0.3-1.2 mils)
Fluidextractum Digitalis, U. S. P. . .	1-2 min. (0.06-0.12 mils)
Infusum Digitalis, U. S. P.	1-2 fl. dr. (4.0-8.0 mils)
Pulvis Digitalis.	½-2 gr. (0.03-0.13 gm.)

Digitoxin (the most irritant of the glucosids, but the most powerful and the most uniform in its effects)— $\frac{1}{200}$ to $\frac{1}{100}$ gr. (0.00032 – 0.00065 gm.).

Digitalin, "German," (a mixture of digitalis bodies, of somewhat variable composition, but containing a large proportion of digitonin). Although moderately irritant, it may be given hypodermically— $\frac{1}{40}$ – $\frac{1}{4}$ gr. (0.0016–0.016 gm.).

Digitalin, "French," (a mixture of digitalis bodies containing a large proportion of true digitalin)— $\frac{1}{250}$ to $\frac{1}{40}$ gr. (0.00026–0.0016 gm.).

Digitalin, "Nativelle," (chiefly digitoxin)— $\frac{1}{240}$ gr. (0.00025 gm.).

Digipuratum is an alcoholic extract of digitalis, free from digitonin and inactive substances, and of the same strength as digitalis leaves. It is prepared in tablet and liquid form, each tablet representing $1\frac{1}{2}$ grains (0.1 gm.) of digitalis and 15 minims, (1 mil) of the liquid being equivalent to $1\frac{1}{2}$ gr. (0.1 gm. of digitalis).

Digalen is said to be a solution of digitoxin in alcohol, glycerin and water, each 15 minims (1 mil) containing $\frac{1}{25}$ gr. (0.0003 gm.) of digitoxin.

The galenic* preparations of digitalis are prone to deteriorate on keeping, the tincture, however, much less rapidly than the infusion or fluidextract.

Pharmacologic Action.—The dominant action of digitalis is on the circulation, the important effects of the drug being (1) slowing of the rate of the heart, (2) strengthening of the systolic contractions, with an increase in the output of the ventricles, and (3) constriction of the vessels in certain large vascular areas.

Vagus Stimulation.—The slowing of the contractions of the whole heart that occurs when digitalis is first introduced into the blood-stream of an intact animal is due chiefly to stimulation of the vagus center. This is shown by the fact that the slowing is very slight or absent if the vagi are divided or are paralyzed by atropin before the digitalis is administered. After a time, if large doses are used, the increased irritability of the cardiac muscle caused by the drug offsets the effect of vagus stimulation. In human beings with a normal pulse-rate or with a frequent pulse the result of acute infection digitalis often fails to exert any inhibitory effect. Not rarely in digitalis intoxication the rate of the ventricles alone is reduced through depression of auriculoventricular conduction.

* Preparations containing one or more of the organic constituents of crude drugs, such as fluidextracts, infusions, tinctures and extracts, are known as galenics, from Galen, the celebrated Roman physician of the second century.

Although the tendency of vagus stimulation is to prolong the diastole and to weaken the systole, and thus to reduce the output of the ventricles, these effects on the efficiency of the heart are more than offset by the powerful stimulating action of the drug on the cardiac muscle. Very large doses of digitalis, by strongly stimulating the inhibitory mechanism of the heart, may also produce arrhythmia (sinus arrhythmia).

Impairment of Conductivity.—Digitalis has a pronounced depressing effect upon the conductivity of the auriculoventricular bundle. This is the result not only of vagus stimulation, which can be neutralized by atropin, but also of a direct action of the drug on the auriculoventricular bundle itself. The effect of the interference with conduction varies from a slight lengthening of the interval between the auricular and the ventricular contractions to partial or complete heart-block. Certain pathological changes in the auriculoventricular bundle apparently favor blocking of the auricular impulses by digitalis. In complete heart-block the rate of the ventricular contractions is usually reduced to about 30 per minute. It is evident, therefore, that digitalis slowing may be due to stimulation of the vagus center or to direct depression of the auriculoventricular bundle. Depression of the auriculoventricular bundle affects, of course, only the rate of the ventricles.

Myocardial Stimulation.—Digitalis acts as a powerful stimulant to the cardiac muscle, increasing both its tonicity and contractility. Although as a vagus stimulant the drug has a tendency to decrease the pumping efficiency of the heart, it actually increases very materially the output of the organ both per beat and per minute by permitting more complete filling of the ventricles in diastole and by greatly strengthening the systolic contractions.

In electrocardiographic records the effect of digitalis upon the heart is first shown by a prolongation of the time of auriculoventricular conduction and by flattening or inversion of the T-wave in one or more leads.

Digitalis also increases the irritability (sensitiveness to stimuli) of the heart muscle and therefore it has some tendency to produce premature beats or extra-systoles. Somewhat frequently in the minor stage of digitalis intoxication the extra-systole with its succeeding compensatory pause occurs regularly after each normal ventricular contraction, thus producing so-called "coupled beats" (pulsus bigeminus) at the apex and wrist.

In the later stages of poisoning the rhythm is not only very irregular from the occurrence of extra-systoles, but the rate is also much accelerated, because the cardiac muscle is rendered so irritable that it is no longer subject to vagus control. At a

still later period the irritability of the heart may be increased to such an extent that at first the auricles and then ventricles pass into a state of fibrillation. In the intact mammal the heart is finally arrested in diastole. On the other hand, the excised mammalian heart and the intact heart of the frog are arrested by digitalis in systole.

It will be obvious from the foregoing that toxic doses of digitalis are capable of producing every known clinical type of cardiac arrhythmia.

Vasoconstriction.—In animals the intravenous injection of digitalis is followed by a distinct elevation of blood pressure. This is due in part to the increased output of the heart, and in part to constriction of the peripheral vessels, for it has been shown that the elevation of pressure is accompanied by demonstrable shrinking in the volume of the splanchnic viscera. The vasoconstriction is peripheral, at least in part, for when digitalis is added to liquid that is being perfused through excised organs the venous outflow is decreased. Moreover, as the constriction occurs in vessels after paralysis of their vasoconstrictor nerve-endings by apocodein and in vessels that have no vasoconstrictor nerves (coronary and pulmonary arteries) it is likely that the drug acts directly on the arterial muscle. The vasoconstrictor center in the medulla, however, appears to play some part in the vasoconstriction, for it has been found that the elevation of blood pressure effected by digitalis is accompanied by less shrinkage of the splanchnic organs if their connections with the central nervous system are first severed. It may be said, therefore, that digitalis raises the blood pressure in normal animals partly through its cardiac action and partly through vasoconstriction, and that the latter, though mainly due to the direct action of the drug on the arterial muscle, is partly the result of stimulation of the vasoconstrictor center.

The vasoconstriction is not uniform throughout the body, indeed, some vessels are scarcely affected by the drug and others are actually dilated. The constriction is most pronounced in the vessels of the abdominal organs. The vessels of the limbs are only slightly constricted and after large doses may be dilated. This dilatation is due partly to the forcible expulsion of blood from the splanchnic area, and partly, perhaps, to a reflex stimulation of the vasodilator center, excited by vasoconstriction of the abdominal vessels (Cushny).

Although digitalis regularly causes an elevation of blood pressure when administered intravenously to animals, it is usually without such effect when given to men, even in very large doses, probably because the drug has no direct action on the blood

vessels of man or because of a more perfect vasomotor regulation in man, whereby vasodilation in one area compensates for vasoconstriction in another. Even in heart disease with evidences of general venous congestion it often causes marked improvement in the patient's condition without increasing the systolic blood pressure. Indeed, if the pressure has been abnormally high it may actually fall owing to improvement in the general circulation. The usual result of a favorable action is an increase in the pulse-pressure* due not any increase of the systolic pressure, however, but to a definite reduction of the diastolic pressure.

Local Action.—Locally, digitalis acts as an irritant. When applied to mucous membranes it gives rise to smarting, redness and swelling and when injected subcutaneously it causes pain and not rarely leads to abscess formation. Of the glucosids, digitoxin is the most irritant and pure digitalin the least irritant.

Alimentary Canal.—Therapeutic doses of digitalis not infrequently cause nausea and vomiting. These symptoms are due not so much to the irritant action of the drug on the mucous membrane of the stomach as to its action on the vomiting center in the medulla, for they occur, as a rule, only after the digitalis has been taken for two or three days, and appear more promptly when the drug is given intravenously than when it is administered by the mouth. According to Hatcher and Weiss, the emesis is not a direct effect, but a reflex, protective in nature, from the action of the drug on the heart itself, for vomiting does not occur when digitalis bodies are directly applied to the center nor does it occur when all the nervous connections between the heart and medulla are cut.

Diarrhea may also follow the administration of digitalis, but it is observed much less frequently than vomiting.

Kidneys.—In health digitalis has no diuretic effect, but in decompensated heart disease with dropsy, oliguria and other signs of general venous congestion it decidedly increases the output of urine. It may be assumed, therefore, that the drug has no direct influence on the kidneys and that its diuretic effect in cardiac disease is the result of an improvement in the general circulation, the relief of venous stasis in the kidneys, and the absorption of dropsical effusions, with consequent hydremia.

Toxic doses of digitalis, probably by irritating the kidneys, occasionally make the urine scanty and bloody.

Nervous System.—The medulla appears to be the only part of the nervous system that is definitely influenced by digitalis. In man even moderate doses may stimulate the vagus center and,

* The pulse-pressure is the difference between the systolic and diastolic pressure.

directly or indirectly, the vomiting center. In animals very large doses also stimulate the vasoconstrictor center and to some extent the respiratory center.

Absorption, Duration of Effects, and Excretion.—Digitalis bodies are absorbed slowly from the alimentary canal, and often 24 or even 48 hours elapse before any pronounced effect on the circulation is observed. Even intravenous injections of the drug may require 15 or 20 minutes to produce their full effects. According to Eggleston, it usually requires from 1 to 2 days to produce complete digitalization with large doses (1 dram—4 mils—of the tincture every 6 hours, day and night) by the mouth, and from 4 to 6 days with small doses (20 to 40 minims—1.25 to 2.5 mils—every 4 hours). Once a decided digitalis effect is secured, however, it often lasts a week or longer after the administration is discontinued. Excretion of the drug occurs partly by the urine and partly by the feces, and is also slow.

Cumulative Action.—The uninterrupted use of digitalis in therapeutic doses is frequently followed after a time by cumulation, the symptoms of which are similar to those resulting from the administration of single toxic doses and may readily be mistaken for those of the primary cardiac condition for which treatment was undertaken. Cumulation probably depends upon tardy excretion and a progressive increase in the amount of the drug that is fixed in the tissues. Nephritis increases the tendency to it. Some patients are able to take digitalis for many weeks without showing any symptoms of cumulation.

Toxicology.—Toxic manifestations not infrequently occur when digitalis is being used clinically. In many cases nausea, vomiting, and headache are the earliest indications of overdosage. Diarrhea is less common. Pronounced slowing of the heart with arrhythmia (excessive vagus stimulation) is also an early phenomenon. At a later period there may be evidences of partial or complete heart-block (interference with auriculo-ventricular conduction) or there may be extreme rapidity of the heart's action, with arrhythmia from extrasystoles, the beats at first often appearing in couples (excessive muscular irritability). Finally, the rhythm may become altogether confused as a result of fibrillary contractions.

Poisoning from the ingestion of a single large dose of digitalis is characterized by gastric disturbance, and a very slow irregular pulse, succeeded by a very rapid and still more irregular pulse, dyspnea, oliguria, extreme muscular weakness and collapse. The mind remains clear until near the end. Death may be preceded by convulsions.

Treatment of Poisoning.—The patient must be kept in the recumbent position at absolute rest, for the slightest exertion may cause sudden arrest of the circulation. It is important to maintain the body temperature by external heat. Atropin in full doses may prove useful in overcoming excessive inhibition and caffein in combating collapse.

Therapeutics.—Digitalis yields the best results in *decompensated valvular disease of the heart*. In this condition it affords relief in various ways: (1) By prolonging the diastole it rests the heart and allows the ventricles to become more completely filled, and by strengthening the systolic contractions it aids in the more complete emptying of the ventricles; these combined effects tending to readjust the inequality in the arterial and venous circulations. (2) By thus correcting the abnormal distribution of blood it promotes diuresis and facilitates the removal of dropsical accumulations, it improves pulmonary ventilation and oxygenation, and puts the stomach, intestines and liver in better condition for digestion and absorption. (3) By driving more blood into the coronary arteries it may permanently influence for good the nutrition of the cardiac muscle. Individual actions of the drug may further add to its value in special conditions. Thus, in auricular fibrillation and auricular flutter its inhibitory effect upon conductivity serves to prevent the excessively numerous contractions arising in the auricle from reaching the ventricle and exhausting it, and in dilatation of the heart with insufficiency of the auriculoventricular valves digitalis may actually lessen the leakage by producing more powerful systolic contractions and thus reducing the size of the mitral and tricuspid rings.

Irrespective of the form or site of the valvular lesion, digitalis produces the most striking effect when there is *auricular fibrillation*. In this condition, which is responsible for, or associated with, at least 60 per cent. of the cases of pronounced heart failure, the pulse is wholly irregular and usually rapid, and symptoms of general venous congestion, such as dyspnea, enlarged liver, edema and oliguria are frequently present. In *auricular flutter*—a condition closely allied to auricular fibrillation—digitalis may also produce excellent results. In *decompensation with a normal cardiac rhythm* digitalis is somewhat less effective, although it is often very useful, even when there is no pronounced frequency of the pulse. Generally speaking, digitalis is much less reliable when the valvular disease is aortic than when it is mitral. In aortic insufficiency prolongation of the diastole favors leakage back into the ventricle; nevertheless, digitalis may be decidedly beneficial if there are evidences of ventricular failure.

In the advanced grades of *chronic degenerative myocardial disease*

without organic valvular defects digitalis is not rarely ineffective or actually harmful, but in the minor degrees of this condition it is usually of service. It is advisable, however, to begin with small doses and to observe carefully its effects. In *acute myocardial disease* with pyrexia, such as occurs in pneumonia and other acute infections, digitalis often fails, but it should be tried, as in some instances it yields good results. The drug has no place in the treatment of *acute endocarditis*, unless this condition is accompanied by definite indications of myocardial insufficiency.

The presence of *partial heart-block* in cases of cardiac decompensation does not necessarily forbid the use of digitalis, but it should always suggest cautious administration, as by further impairing conduction the drug may make the block complete. If heart-block is already complete digitalis can add nothing to the existing depression of auriculoventricular conduction and may do good by increasing the strength of the ventricular contractions and improving the circulation.

Although digitalis has some tendency to excite *extrasystoles*, the occurrence of these premature beats is not a contraindication, if other conditions are also present in which the drug is likely to be of service. Digitalis rarely affects the pulse rate in *paroxysmal tachycardia*. In *neurogenic (sinus) arrhythmia* its use is inadmissible.

High blood pressure does not in itself contraindicate the use of digitalis; indeed, when the heart is overborne by the excessive labor in this condition and gives evidence of yielding, the administration of the drug may prove a valuable adjunct to eliminative and dietetic measures and rest.

Neither *aneurysm of the aorta* nor *arteriosclerosis* should be considered a bar to the use of digitalis, if its employment is dictated by changes in the heart itself.

As a diuretic digitalis is frequently used to aid in the removal of *edema* from various causes. It is not likely to be of service, however, unless the dropsical effusion is caused by heart-failure, as it influences the kidneys only through its circulatory actions.

Administration.—For administration by the mouth a good standardized tincture, a freshly prepared infusion and powdered digitalis leaves are, as a rule, the best preparations. Powdered digitalis, although slightly more irritant than the liquid preparations is suitable for pills or capsules. The fluidextract is unreliable. Nativelle's digitalin and digipuratum are effective commercial preparations. The larger of Nativelle's granules ($\frac{1}{240}$ grain–0.00025 gm.) is equivalent to about 15 minims (1.0 mil) of the tincture. For intramuscular injection or intravenous injection digitalin "German" or, better, liquid digipura-

tum may be employed. Whatever the preparation, it should be pushed until the desired effect is obtained or signs of intolerance appear. From 15 to 20 minims (1.0–1.25 mls) of the tincture three or four times a day will usually be sufficient. Greater frequency of administration than every fourth hour has no advantages. When prompt digitalization is required 1 dram (4.0 mls) of the tincture may be given every 6 hours, day and night, for four doses and followed by ordinary doses at shorter intervals (Eggleston).

If nausea, vomiting, diarrhea, headache or “coupling of beats” occurs the administration of the drug should be discontinued until the untoward symptom has disappeared. Otherwise it should be continued until full digitalization is secured or until the pulse-rate falls to about 70, when it should be stopped for a few days, and then, if necessary, resumed in smaller doses, the amount being changed from time to time in order to determine the exact dose that will remove the symptoms of heart-failure or afford the maximum degree of improvement without producing a toxic effect. In auricular fibrillation it is usually necessary for the patient to continue the use of drug more or less regularly for the remainder of his life.

In valvular disease with marked *dropsy* digitalis is often used in combination with other remedies, as in the well-known Guy’s (Baillie’s) pill:

℞ Pulveris digitalis,
Pulveris scillæ
Massæ hydrargyri. ʒā gr. xx (1.3 gm.).—M.
Fiant pilulæ, No. xx.
Sig.—One thrice daily after meals.

A good diuretic effect may be obtained with caffein or theobromin. Trousseau’s wine, also, is an effective combination:

℞ Junip. contus. ʒx (40.0 gm.);
Pulv. scillæ. ʒj (30.0 gm.);
Pulv. digitalis. ʒj (4.0 gm.);
Vin. xerici. Oj (½ liter).
Macerate for four days and add:
Potass. acetatis. ʒiij (12.0 gm.).—M.
Express and filter.
Sig.—Tablespoonful three times a day.

STROPHANTHUS, U. S. P.

Strophanthus is the seed of *Strophanthus Kombé* or *Strophanthus hispidus*, climbing plants of Eastern Africa. Its activity depends upon a glucosid or a mixture of glucosids, *strophanthin*, a white or yellowish powder, readily soluble in water or in diluted

alcohol. Ouabain (crystalline strophanthin, gratus strophanthin), a glucoside from the wood of *Acocanthera Ouabaio* or the seeds of *Strophanthus gratus*, has an action similar to that of the amorphous or official strophanthin, but it is about twice as toxic. It is also rather sparingly soluble in water.

PREPARATIONS

DOSE

Tinctura Strophanthi, U. S. P.....	5-15 min. (0.3-1.0 mil)
Strophanthinum, U. S. P.....	Mouth, $\frac{1}{60}$ gr. (0.001 gm.);
Ouabain (crystalline strophanthin)...	intravenous or intramuscular injection, $\frac{1}{80}$ gr. (0.00075 gm.)
	One-half the dose of official strophanthin.

Pharmacologic Action.—Strophanthus has an action similar to that of digitalis, but it is very much more toxic to the muscle of the heart, less certain of absorption from the digestive tract, and when administered by the mouth much less reliable. Although less irritant than digitalis, it seems more prone than the latter to produce diarrhea. However, in the form of strophanthin, administered by intravenous or intramuscular injection, it is often very effective, acting more promptly than digitalis, although somewhat less persistently. In animals strophanthus appears to have less constricting effect on the vessels than digitalis.

Therapeutics.—Strophanthus may be used in the class of cases in which digitalis is indicated, but it is much less reliable. Although its absorption is usually poor, it is occasionally rapid, and hence serious poisoning may occur even from ordinary doses. However, in sudden heart failure, especially in cases of auricular fibrillation, a striking effect is sometimes produced by injecting strophanthin into a muscle or preferably into a vein, the patient being tided over until digitalis, orally administered, has had time to act. The dose, $\frac{1}{80}$ grain (0.00075 gm.) of the official preparation, dissolved in 2 drams (8 mils) of normal salt solution, should be given at once and not repeated before 48 hours. If ouabain is employed the dose should be $\frac{1}{160}$ grain (0.0004 gm.) or less, dissolved in normal salt solution in the proportion of 1 to 6000. Under no circumstances should strophanthin or ouabain be given by intravenous or intramuscular injection if the patient has been taking digitalis by the mouth, unless 3 or 4 days at least have elapsed since the last dose of digitalis, as the combined effect of the two drugs is likely to result in ventricular fibrillation and death. In case of doubt the initial dose of strophanthin should not exceed $\frac{1}{130}$ grain (0.0005 gm.).

Rahn has collected 25 cases of death occurring in close connection with the injection of strophanthin and believes that many of

the fatalities might have been prevented with smaller doses, longer intervals, and a better knowledge of the patient's previous medication, especially as to digitalis.

CONVALLARIA

(Lily of the Valley)

Convallaria is the rhizome and roots of *Convallaria majalis*. It contains two glucosids, *convallarin* and *convallamarin*.

Convallarin, being a saponin (see p. 20), is not absorbed from the alimentary canal, and, therefore, the value of the drug as a cardiac stimulant depends chiefly upon the convallamarin.

PREPARATIONS	DOSE
Fluidextractum Convallariæ.....	5-20 min. (0.3-1.2 mls).
Convallamarin.....	½-1 gr. (0.03-0.065 gm.).

Pharmacologic Action.—Convallaria has an action on the heart similar to that of digitalis, but is poorly absorbed and unreliable.

ADONIDIN

Adonidin is a glucosid obtained from the *Adonis vernalis*, a perennial plant indigenous to Central Europe and Asia. It is a hygroscopic, odorless, bitter powder, soluble in water and in alcohol. The dose is from $\frac{1}{12}$ to $\frac{1}{4}$ grain (0.005-0.015 gm.).

Pharmacologic Action.—Adonidin has a digitalis-like action, but it is poorly absorbed from the gastrointestinal and is, therefore, unreliable.

OTHER CIRCULATORY STIMULANTS*

Squill (see p. 287).—Squill has a digitalis-like action, but it is more irritant to the stomach than digitalis and much less certain of absorption. Poisoning is rare, even with very large doses. The drug produces diuresis in cardiac decompensation with edema by improving the circulation, but it has no direct stimulating effect upon the kidneys. Owing to its pronounced irritant action on the stomach, it was at one time used in large doses as an emetic. In comparatively small doses it is still a favorite expectorant.

In *myocardial insufficiency* squill is chiefly employed at present as an adjuvant to digitalis when there is persistent *dropsy*. In such cases the combination of powdered squill, powdered digitalis, and blue mass, known as Guy's Hospital pill, is commonly prescribed. Its combined expectorant and digitalis-like prop-

* The properties of these drugs are more fully considered under other headings.

erties make it of value in some cases of *bronchitis* with *emphysema* and *weak heart*, occurring in elderly persons.

Apocynum (Canadian Hemp).—This drug has the same qualitative action as *digitalis*, but it is more irritant to the digestive tract and less certain of absorption. The fluidextract is sometimes given in doses of from 5 to 15 minims (0.3–1.0 mil) in *valvular disease* when there is much dropsy, but it is prone to excite vomiting or diarrhea.

Cactus Grandiflorus.—This drug has been employed for a number of years as a substitute for *digitalis* in various functional and organic diseases of the heart. The experimental evidence, however, does not support the view that it has a *digitalis*-like action, nor are clinicians in accord as to its therapeutic value. It is usually prescribed in the form of a fluidextract made of the fresh plant, the dose of which is from 10 to 30 minims (0.6–2.0 mils).

Caffein (see p. 240).—While caffein is entitled to consideration as a cardiac stimulant, its action is very different from that of *digitalis* and its allies. It stimulates the heart muscle directly, and thus increases the force of the systolic contractions, but as it does not prolong the diastolic relaxation, it does not materially increase the volume of blood that is discharged from the ventricle during each systole. Its action is more prompt than that of *digitalis* but less persistent. As a diuretic, caffein may be even more effective than *digitalis*, as, unlike the latter, it has a direct action on the kidney, although it is not definitely known whether the seat of this action is the renal parenchyma itself or the renal vessels. Finally, caffein has more side-actions than *digitalis*, large doses not infrequently producing palpitation, excitement, sleeplessness and gastrointestinal disturbances. As an adjuvant to *digitalis*, caffein may be employed with advantage in *valvular heart disease when dropsy is a prominent feature*. In the *circulatory failure of the acute infections* it is sometimes more effective than *digitalis*.

Strychnin (see p. 148).—Therapeutic doses of strychnin have no direct effect upon the heart and very little upon the vasoconstrictor center, and clinically, increase of bloodpressure is rarely observed after its use; nevertheless the drug is often of value in the *circulatory failure of acute infections* and in some cases of *chronic myocardial disease*, especially the *muscular insufficiency incident to old age*. It is likely that the good effects are due to improvement in the general muscular tonus brought about by the action of the drug on the central nervous system. In the *circulatory failure of the acute infections* it should be given freely, but not too continuously.

Epinephrin and Pituitary Extract (see pp. 59 and 63).—When administered intravenously epinephrin and pituitary extract (posterior lobe) produce a marked but transitory elevation of bloodpressure with some slowing of the pulse. These effects are much less pronounced with intramuscular injection, and are not observed at all after subcutaneous or oral administration. The chief factor in the elevation of bloodpressure is intense vasoconstriction, brought about in the case of epinephrin by stimulation of the vasoconstrictor nerve-endings and in the case of pituitary extract by direct stimulation of the arterial muscle. The slowing of the pulse is due mainly to stimulation of the vagus center by the increased bloodpressure, although that occurring from pituitary extract may be due in part also to depression of the heart itself. As circulatory stimulants these drugs are chiefly useful in temporarily raising the bloodpressure in *collapse*, *traumatic shock*, and *poisoning* by cardiac depressants. Intravenous injections should be made slowly, the remedy being well diluted with normal salt solution. If injected too rapidly or in too concentrated solution either drug may constrict the vessels so powerfully as to cause dilatation of the heart and pulmonary edema. Owing to their transitory action and the necessity of administering them by intravenous or intramuscular injection, epinephrin and pituitary extract are only serviceable in emergencies.

Ammonia (see p. 282), **Alcohol** (see p. 130) and **Ether** (see p. 117).—In therapeutic doses these drugs have little or no direct action on the heart, but through their local irritant effects they reflexly stimulate the heart and the medullary centers, thus tending to increase the pulse-rate, raise the bloodpressure, and improve the respiration. The action is very prompt, but the effects are slight and transitory. Clinically, these so-called diffusible stimulants are useful in various forms of *sudden circulatory failure*, such as syncope, shock, and acute myocardial insufficiency resulting from infectious disease or poisoning. Ammonia gas may be inhaled from ammonia water (aqua ammoniæ) or smelling salts, or 20 minims (1.25 mls) of the aromatic spirit of ammonia, more or less diluted, may be given by the mouth. Alcohol is best given in the form of whisky or brandy. Four fluidrams (15 mls) may be given by the mouth, undiluted and preferably hot, and repeated, if necessary. Ether should be administered hypodermically in doses of from 15 to 20 minims (1.0–1.25 mls), repeated in fifteen minutes, if necessary.

Camphor (see p. 141).—There is little experimental evidence to support the view that camphor has any decided action on the

heart, either direct or indirect; nevertheless clinical experience seems to show that it is sometimes useful as a quickly acting stimulant in *acute infectious diseases*, especially pneumonia, when circulatory collapse is imminent. It should be given hypodermically in doses of from $\frac{1}{2}$ to 3 grains (0.03–0.2 gm.), dissolved in sterile olive oil, and repeated every two hours.

CIRCULATORY DEPRESSANTS

Circulatory depressants are drugs which decrease the efficiency of the heart. Many of them act by directly depressing the cardiac muscle. As examples of this type may be mentioned:

Hydrated chloral

Chloroform.

Potassium salts when administered intravenously in such doses as to produce a concentration of 0.08 per cent. or more in the blood also powerfully depress the heart. Ordinary doses by the mouth, however, have no such effect. Contrary to common belief, the analgesic benzol derivatives (salicylic acid, acetylsalicylic acid, antipyrin, acetanilid, etc.), are not, in ordinary doses, active cardiac depressants, although in the presence of individual idiosyncrasy or sensitiveness, which is by no means uncommon, they depress the vasomotor system and produce collapse. The circulatory weakness that is not infrequently observed after their use in febrile diseases is probably due more to the abrupt defervescence itself than to any direct depression of the heart or vasomotor center. The continuous use of "headache powders" is justly condemned, however, for it is likely to result in deterioration of the blood (methemoglobinemia) and cardiac and vasomotor depression.

Other circulatory depressants act chiefly by stimulating the inhibitory mechanism of the heart. The most important members of this group are:

Aconite

Veratrum viride.

These drugs in the intact animal stimulate the vagus center and thus prolong the diastolic pause and weaken the ventricular contractions. As these effects upon the heart are not offset by any pronounced stimulation of the cardiac muscle, as is the case with digitalis and its allies, the tendency is to decrease the output of the ventricles both per beat and per unit of time.

Reduction of Bloodpressure.—The bloodpressure may be lowered (1) by decreasing the quantity of fluid in the vessels (venesection); (2) by decreasing the output of the heart (cardiac depressants and pure vagal stimulants); and (3) by decreasing the resistance in the arterioles (general vasodilators).

Drugs that dilate only the vessels of the skin, such as alcohol in therapeutic doses and antipyrin, do not change the general blood pressure, as the peripheral vasodilation is compensated for by constriction of the splanchnic vessels.

Reduction of the Pulse-rate.—The action of the heart may be slowed (1) by directly stimulating the inhibitory mechanism in the medulla (*digitalis*, *aconite*, *veratrum viride*); (2) by raising the blood pressure and thus indirectly stimulating the inhibitory mechanism in the medulla (*epinephrin*); by depressing the heart itself or its accelerator mechanism (*chloroform* and *chloral* in large doses).

Indications for Using Circulatory Depressants.—The only drugs that are ever used as circulatory depressants are those which act by stimulating the vagus, namely, *aconite* and *veratrum viride*, and even for these the indications are few. Occasionally, such drugs are of service in controlling overaction of the heart in the early stages of sthenic infections, in reducing tension in the aorta in aneurysm, and in lowering blood pressure in certain forms of hyperpiesis. Cardiac weakness from any cause is an absolute contraindication.

ACONITUM, U. S. P.

(Monkshood)

Official *aconite* is the root of *Aconitum Napellus*, a perennial herb growing in Europe, Asia, and North America. The root is conical in shape, 2 or 3 inches long, brownish in color, and resembles horse-radish, from which it may be distinguished, however, by its lack of pungent odor when scraped. When slowly chewed, it produces a sense of warmth and tingling in the mouth, soon followed by numbness.

The most important principle of *aconite* is *Aconitin* (*Aconitina*, U. S. P.), a crystalline alkaloid, very slightly soluble in water but more freely so in alcohol and dilute acids. The amorphous *aconitin* of commerce is a mixture of alkaloids of variable strength, but weaker than the official preparation. The dose of crystalline *aconitin* is from $\frac{1}{600}$ to $\frac{1}{300}$ grain (0.0001–0.0002 gm.).

PREPARATIONS

DOSE

Tinctura Aconiti, U. S. P.	5–15 min. (0.3–1.0 mil)
Fluidextractum Aconiti, U. S. P.	1–2 min. (0.06–0.12 mil)
Extractum Aconiti, U. S. P.	$\frac{1}{8}$ – $\frac{1}{4}$ gr. (0.008–0.016 gm.)
Līnimentum Aconiti.	

Pharmacologic Action.—**Local Action.**—*Aconitin* in aqueous solution is not absorbed from the unbroken skin, but if rubbed in with fat, alcohol, or chloroform it produces first a

tingling sensation, then numbness, and, finally, partial anesthesia. It is readily absorbed from all mucous membranes, so that the merest trace when applied to the tongue produces almost immediately the characteristic numbness and tingling. Even large doses by the mouth or subcutaneously may produce the same phenomena in the tongue, lips, throat and finger-tips. This peculiar effect of aconitin upon the mucous membranes and skin is the result of its selective action on the sensory nerve-endings. These are first stimulated and then depressed. Even in concentrated form the drug does not cause redness or other signs of inflammation.

Circulatory System.—From a therapeutic viewpoint the dominant circulatory action of aconite is on the vagus. Full therapeutic doses slow the pulse-rate and lower the blood pressure by stimulating the vagus center. These effects can be offset by section of the vagi or paralysis of the vagi by atropin.

Toxic doses greatly increase the irritability of the cardiac muscle; first increase the force of the ventricular contractions and then weaken them; first slightly stimulate the vasomotor center and then depress it; the effects being marked acceleration of the beats, with extreme arrhythmia (extrasystoles and eventually fibrillation), and a rapid fall in the blood pressure. Death may be due to cardiac paralysis or to arrest of the respiration.

With ordinary doses the actions of aconite on the cardiac muscle are entirely subordinate to central vagus stimulation.

Effects of Aconite and Digitalis upon the Circulation Compared.—Both drugs in full doses stimulate the vagus center and thus tend not only to prolong the diastolic pause, but also to weaken the systolic contractions and thereby reduce the output of the ventricles. *Digitalis* by powerfully stimulating the cardiac muscle, however, more than offsets the effects of inhibition upon the systolic contractions and consequently increases the output of the ventricles. With *aconite*, on the other hand, the effect of ordinary doses is almost one of pure inhibition, the direct action of the drug on the heart itself not coming into play except after toxic doses.

Respiration.—After large doses of aconite the breathing becomes slower, more labored, and sometimes dyspneic, these phenomena being due apparently to direct depression of the respiratory center. In fatal poisoning death is sometimes the result of paralysis of the respiratory center.

Nervous System.—Apart from its action on the medullary centers (vagus, respiratory and vasomotor), aconite does not seem to have any important influence on the central nervous system. The convulsions sometimes seen after toxic doses are

probably the result of asphyxia or cerebral anemia. In poisoning the mind generally remains clear until near the end, although occasionally unconsciousness occurs early from collapse. With strong concentrations, the endings of the motor nerves, as well as those of sensory nerves, are apparently first stimulated and then depressed.

Secretions.—It is doubtful whether aconite has any direct action on the nerve-endings of the secretory glands. The excessive flow of mucus following the introduction of the drug into the nostrils or mouth is excited reflexly by irritation of the sensory nerve-endings, and the free perspiration observed in poisoning is probably the result of collapse.

Digestive Tract.—Toxic doses of aconite not rarely cause nausea and vomiting, probably by stimulating the vomiting center in the medulla. Therapeutic doses are without influence.

Temperature.—Aconite lowers temperature to some extent, both in health and in febrile states, but the manner of its antipyretic action is not definitely known. It is believed, however, that the drug acts partly by depressing the circulation and partly by influencing directly the heat-coördinating centers.

Toxicology.—The symptoms develop very rapidly after the ingestion of the poison. Among the first to appear is the characteristic tingling, which, beginning in the lips, tongue, and throat, soon spreads to the fingers and toes, and at last involves the whole surface. This is accompanied by chilliness, muscular weakness, salivation and sometimes by nausea and vomiting. The pulse, at first infrequent and soft, later becomes extremely frequent, weak, and irregular. The breathing is slow and labored. The skin is cool, livid, and covered with sweat. The mind is usually clear until near the end, but sometimes unconsciousness occurs rather early in consequence of the profound collapse. Death is often preceded by convulsions. It may be due either to cardiac or to respiratory paralysis.

Treatment.—This consists in evacuating the stomach, if necessary; in practicing artificial respiration; in maintaining the body-temperature by external heat; and in combating respiratory and cardiac failure by subcutaneous injections of atropin, ammonia and strychnin. The artificial respiration and administration of atropin, which in several respects is antagonistic to aconite, are probably the most potent measures. Throughout the treatment it is essential to keep the patient recumbent, with the head a little lower than the feet.

Therapeutics.—In acute inflammatory diseases of the upper respiratory tract, such as *pharyngitis*, *tonsillitis*, *laryngitis* and *bronchitis*, and the early stages of *acute sthenic infections*, such as

scarlatina, aconite may be useful as a circulatory sedative and mild antipyretic. In the *functional overaction of the heart*, sometimes seen in neurotic subjects, it may also be of service, but it must be used with care. The liniment of aconite, official in the British Pharmacopœia, sometimes affords relief in *myalgia*. An ointment of aconitin—5 to 10 grains (0.3–0.6 gm.) to the ounce (30.0 gm.)—was formerly used as a local analgesic in *neuralgia*, but its employment is by no means free from danger.

Administration.—The tincture is the best preparation for internal use. Small doses should be given at frequent intervals and the effects carefully observed. Aconitin, owing to its great toxicity, should be avoided. The following time-honored combination is efficacious in the mild febrile infections of childhood.

℞. Tincturæ aconiti..... ℥xii (0.75 mil)
 Spiritus ætheris nitrosi..... f ℥ vi (22.0 mls)
 Liquoris potassii citratis q. s. ad f ℥ iii (90.0 mls).—M.
 Sig.—A dessertspoonful every two hours for a child of three years.

For *acute laryngitis* in childhood the following may be used.

℞. Tincturæ aconiti..... ℥x (0.6 mil)
 Tincturæ opii camphoratæ..... f ℥ iss (6.0 mls)
 Syrupi ipecacuanhæ..... f ℥ ij (8.0 mls)
 Liquoris potassii citratis.. q. s. ad f ℥ iii (90.0 mls).—M.
 Sig.—Two teaspoonfuls every three hours for a child of three years.

VERATRUM VIRIDE, U. S. P.

(Green Hellebore, American Hellebore)

Veratrum viride is the dried rhizome and roots of *Veratrum viride*, a lilaceous plant growing in North America. It is closely related to *Veratrum album*, or white hellebore, found in Europe and Asia, but it is in no way related to black hellebore (*Heleborus niger*). It contains a number of alkaloids, the most important of which is apparently *protoveratrin*.

PREPARATIONS

DOSE

Tinctura Veratri Viridis, U. S. P. 5–15 min. (0.3–1.0 mil)
 Fluidextractum Veratri Viridis, U. S. P. 1–3 min. (0.06–0.2 mil).

Pharmacologic Action.—*Veratrum viride* has actions similar to those of aconite, but it is somewhat more irritant to mucous membranes and somewhat less stimulant to sensory nerve-endings. In full dose it slows the heart-rate and lowers the bloodpressure, these effects being due chiefly to stimulation of the vagus center. Toxic doses after first slowing the pulse, suddenly accelerate it and at the same time cause pronounced arrhythmia and a fall in the blood pressure. Like aconite, verat-

rum viride also lowers temperature. The vomiting constantly observed in poisoning by veratrum viride is due partly to irritation of the gastric mucosa (reflex), but it is chiefly a central effect.

Special Actions of Protoveratrin.—Protoveratrin has an action on the circulation similar to that of aconitin, but is less toxic. It is also a more certain emetic. Like cevadin (veratrin, see p. 174) it acts directly on the muscle substance, causing somewhat more prompt and more powerful contractions. The contractions, however, are not prolonged as with cevadin, and the muscle rapidly becomes fatigued.

Therapeutics.—Veratrum viride is used internally in the same class of cases as aconite. It has been especially recommended in *puerperal eclampsia* to lower the bloodpressure and to check the convulsions. In doses of 10 minims (0.6 mil) every three hours, its effects being carefully observed, it is sometimes a useful addition to other remedies. In *thoracic aneurysm*, when there is much pain and the cardiac contractions are strong, veratrum viride, in conjunction with potassium iodid and rest, may afford relief.

Contraindication.—Veratrum is contraindicated in cardiac weakness from any cause.

Administration.—The tincture is the best preparation; it should be given at frequent intervals, the dose being cautiously increased until physiologic effects are produced.

OTHER CIRCULATORY DEPRESSANTS

Veratrina, U. S. P.—Veratrina is a mixture of *cevadin* with a number of less active alkaloids, obtained from the seed of *Asagrae officinalis*, a liliaceous herb growing in Mexico and Central America.

Cevadin has an action on the circulation similar to that of aconitin and protoveratrin, its toxicity however being less than that of either of these alkaloids. It affects the sensory nerve-endings like aconitin, but unlike the latter it is a powerful irritant to the skin and mucous membranes. It has also a characteristic action on striped muscle. Under its influence, the muscle contracts as rapidly as usual, but more vigorously, and once contracted, requires from 20 to 30 times the normal time to relax again. Further, the drug increases the irritability of muscle and restores to some extent its contractility, when this has been lost through fatigue. The action of cevadin is probably on the muscle substance itself, as it occurs after the motor nerve-endings have been paralyzed by curare. Strong concentrations depress the motor nerve-endings without, however, first stimulating them.

Therapeutics.—Veratrin is used only as a counterirritant. In the form of an ointment (4 per cent.), it has been recommended as a local remedy in *neuralgia*. It should never be applied over large areas or where there are any abrasions, and in employing it about the face great care must be taken to keep it out of the eye.

Stavesacre.—This drug (*Staphisagria*, U. S. P.) is the seed of *Delphinium Staphisagria*, an annual herb growing in Southern Europe. It contains several alkaloids, the chief of which is *delphinin*. The United States Pharmacopœia recognizes a fluidextract (*Fluidextractum Staphisagriae*). The action of stavesacre is similar to that of aconite, but the drug is rarely used at present except externally for the destruction of *pediculi* on the head or pubic hair. For this purpose an ointment of the crushed seed (20 per cent.) or the fluidextract with diluted acetic acid may be prescribed.

R. Fluidextracti staphisagriae. f ʒii (8.0 mls)
Acidi acetici diluti. f ʒiv-f ʒvi (120.0–180.0 mls).—M.

VASOCONSTRICTORS AND VASODILATORS

Vasoconstrictors are drugs that contract the arterioles. They may act (1) by stimulating directly or reflexly the vasoconstrictor center in the medulla, (2) by stimulating the vasoconstrictor (sympathetic) nerve-endings or the myoneural junctions, or (3) by stimulating directly the muscular tissue of the vessels.

The vasoconstrictor effect of a drug may be considered to be peripheral if it occurs after the central nervous system has been destroyed, if it occurs in segments of excised arteries, or if a solution of the drug when perfused through an isolated viscus decreases the venous outflow. It may be inferred that the vasoconstricting effect of the drug is directly on the arterial muscle itself if it occurs after the vasomotor nerve-endings have been paralyzed by ergotoxin or apocodein.

Digitalis and allied drugs have a vasoconstrictor action, which is chiefly peripheral, but the effect of this action is not seen in man, either in health or disease. Ergot, injected intravenously, raises the blood pressure through vasoconstriction. The action is peripheral, for it occurs after section of the splanchnic nerves and also on perfusion of an isolated viscus. It depends upon the active principles, ergotoxin and tyramin, and is probably due to stimulation of the arterial muscle itself and the sympathetic nerve-endings. However, in large doses, ergotoxin, the

most important of the alkaloids of ergot, paralyzes the vasoconstrictor nerve-endings, leaving the dilator mechanism active.

Cocain, atropin, caffein, and picrotoxin have a stimulant action on the vasoconstrictor center, but the effect upon the bloodpressure is slight, and in the case of caffein almost entirely offset by peripheral vasodilation. Alcohol, ether and ammonia, through their irritant properties, may cause a reflex stimulation of the vasoconstrictor center, with contraction of the splanchnic vessels and a rise in the arterial pressure. The effect of these drugs, however, is slight and transitory.

The most powerful vasoconstrictors known are:

Epinephrin and Pituitary Extract (Posterior Lobe).

The action of both epinephrin and pituitary extract is mainly peripheral, that of the former apparently being on the vasoconstrictor nerve-endings or the myoneural junctions and that of the latter on the arterial muscle itself. Vasoconstrictors raise the general blood pressure and by increasing the tonus in the medulla tend to lessen the frequency of the heart's action and to stimulate the respiration. As internal remedies they are especially indicated in conditions of low arterial tension, such as collapse and shock. Mild cutaneous stimulation, as by heat or mustard, may be used in conjunction with these drugs, as it also tends to produce general vasoconstriction.

Vasodilators are drugs that dilate the arterioles. They may act (1) by depressing the vasoconstrictor center, (2) by depressing the vasoconstrictor nerve-endings, (3) by stimulating vasodilator nerve-endings, or (4) by depressing directly the muscular tissue of the vessels.

Alcohol and chloral in large doses and chloroform even in light anesthesia dilate the vessels and lower the blood pressure through central vasomotor depression. Ergotoxin and apocodein in large doses act peripherally as vasodilators by depressing the vasoconstrictor nerve-endings and are employed for this purpose in experimental work. Epinephrin under certain conditions, especially late in the course of perfusion, secondarily dilates the vessels, probably by stimulating the vasodilator mechanism. Even when administered intravenously to intact animals this drug may so powerfully constrict the splanchnic vessels, which are especially sensitive to it, as to cause passive dilatation of certain peripheral arteries by displacement of blood.

The purest and most powerful of the vasodilators are those which directly depress the arterial muscle. To this group belong:

The Nitrites	{	Amyl nitrite	{	Nitroglycerin
		Ethyl nitrite and The Organic Nitrates		Erythrol tetranitrate
		Sodium nitrite		

Benzyl benzoate and *papaverin*, an alkaloid of opium (see p. 98),¹ also have a peripheral vasodilator action, but they are recommended especially for relaxing spasmodically contracted viscera.

Vasodilators, especially those that are relatively free from side-actions, are employed to reduce the bloodpressure in cases of hyperpiesis, to relax the coronary arteries in paroxysms of angina pectoris, and to facilitate the passage of blood through the vessels in certain cases of myocardial insufficiency.

EPINEPHRIN

(Adrenalin)

Epinephrin is the active principle of the medulla of the suprarenal gland. It has the properties of an alkaloid and with acids forms soluble salts. It is usually marketed in the form of an aqueous 1:1000 solution of the hydrochlorid, preserved with some antiseptic. On exposure to air, on dilution, or even on long standing this solution gradually deteriorates, acquiring a reddish color. The average dose is 10 minims (0.6 mil). The alkaloid itself is rarely employed.

Pharmacologic Action.—Circulatory System.—When injected into a vein, even in small doses, epinephrin causes a sudden and marked rise of bloodpressure, with slowing and strengthening of the heart-beats. Similar, but less pronounced, effects are also observed after intramuscular injections of the drug. The rise of bloodpressure is due mainly to constriction of the arterioles, especially those of the splanchnic area, but partly also to increased force of the heart; the slowing of the heart-beats is due to stimulation of the vagus center in the medulla by the rise of bloodpressure, and not to direct stimulation of the vagus, for it does not occur when the vasoconstrictor effect is overcome by ergotoxin; and the increased force of the heart-beats is probably due to stimulation of the cardiac accelerator (sympathetic) mechanism. The vasoconstriction occurs after destruction of the central nervous system and, therefore, must be of peripheral origin. It is apparently due to stimulation of the vasoconstrictor nerve-endings or the myoneural junctions, for it can be abolished by ergotoxin, and is slight or wanting in vessels the vasomotor innervation of which is doubtful. It has been shown that relaxed

vessels are more responsive to epinephrin than those in normal contraction. Intense local contraction of the arterioles is observed even when the drug is directly applied to mucous membranes or raw surfaces. Overdoses of epinephrin intravenously, or even the too rapid injection of a normal dose, may cause such intense vasoconstriction as to bring about dilatation of the left ventricle and pulmonary edema.

The effects of the drug on the general circulation are not noticeable after administration by the mouth, and are very slight after subcutaneous injection. Even after intravenous or intramuscular injection they are fugitive, lasting but a few minutes, unless the administration is continuous or nearly so. This marked variation in the effects of epinephrin with different methods of administration is to be ascribed to its slow absorption, on the one hand, and to its rapid oxidation on the other.

Epinephrin apparently stimulates the vasodilators as well as the vasoconstrictors, although the action on the latter usually predominates. Vasodilation, however, may sometimes be observed with very dilute solutions and also as a secondary effect after vasoconstriction has disappeared. Certain vessels which are but little influenced by the vasomotor actions of the drug, such as the pulmonary arteries, may be passively dilated by the displacement of blood from areas of pronounced constriction.

Josué and others have shown that repeated intravenous injections of epinephrin in rabbits are sometimes followed by degenerative changes in the aorta and larger arteries resembling atheroma. Whether these changes are the result of a direct toxic action or of the increased blood pressure has not been definitely determined. They do not occur in dogs or monkeys, and it is very doubtful whether they occur in man.

Local Action.—Upon the unbroken skin epinephrin is without effect, but when applied to denuded surfaces or to any of the mucous membranes, even in very dilute solution, it blanches and shrinks the tissues of the part through its powerful vasoconstricting action. As the ischemia disappears it is replaced by hyperemia and relaxation of the tissues, in consequence of the secondary vasodilator action of the drug.

Nervous System.—The dominant action of epinephrin is stimulation of the sympathetic endings, the effect of the drug upon a given organ varying according as the sympathetic innervation of the organ is augmentory or inhibitory. Thus, on the one hand, it causes constriction of most of the arteries, stimulation of the accelerator mechanism of the heart, and dilatation of the pupil, and on the other hand, relaxation of the bronchioles and weakening of the rhythmic movements in the stomach, intestine,

and gall-bladder. The drug has no important action on the central nervous system or on the sensory or motor nerves.

Respiratory System.—The respiratory center is affected only indirectly through changes in the blood pressure. Although subcutaneous injections of epinephrin have little effect upon the blood vessels, they are quite sufficient to overcome excessive contraction of the bronchioles by stimulating the bronchodilator (sympathetic) nerve-endings.

Digestive Tract.—When taken by the mouth epinephrin is absorbed so slowly that it is destroyed before it reaches the blood, and so is without systemic effect. In the stomach, however, it may act as a local vasoconstrictor. Administered intravenously it tends to relax the stomach, intestines and gall-bladder, to decrease gastrointestinal peristalsis, to increase saliva and mucous secretions, and to decrease the external secretion of the pancreas (effects of sympathetic stimulation). In animals large doses of epinephrin cause glycosuria and increase the glycosuria occurring in diabetes; further, Bernard's piqure is without power to produce glycosuria after the removal of the adrenals or division of the left splanchnic, which supplies both adrenals. It is likely, therefore, that the function of the adrenals is opposed to that of the pancreas and that epinephrin favors the mobilization of sugar by stimulating the sympathetic endings in the liver.

The Eye.—Dropped into the eye, the solution of epinephrin produces the effects of sympathetic stimulation, namely, pallor of the mucosa, widening of the palpebral angle and slight exophthalmos. Dilatation of the pupil, however, does not usually occur in man, unless the sympathetic system is especially sensitive, as in cases of hyperthyroidism.

The Uterus.—The action of epinephrin on the uterus is not uniform in all animals. In human beings it tends to produce uterine contractions or to increase them, if already present, by stimulating the hypogastric (sympathetic) nerve, even when given subcutaneously. As a uterine stimulant it is inferior to pituitary extract.

The Secretions.—The tears, saliva, and mucus are increased by stimulation of the sympathetic nerve-endings. As in man the sweat-glands respond chiefly to parasympathetic stimulation, the sweat is not increased.

Toxicology.—In animals very large doses of epinephrin cause excitement, tremors and vomiting, followed by paresis of the hind limbs and death from cardiac or respiratory paralysis.

Therapeutics.—As a peripheral vasoconstrictor epinephrin is of great value in arresting *capillary hemorrhage* in any part with

which it can be brought in contact, such as the mucous membrane of the nose, stomach, rectum or bladder. Solutions of from 1:10,000 to 1:1000 may be used for the purpose. In *epistaxis* the solution may be used as a spray or on a tampon. In *hematemesis* from 30 to 60 minims (2.0–4.0 mils) of the 1:1000 solution in a tablespoonful of water may be given every twenty minutes or half hour. Suppositories containing $\frac{1}{65}$ grain (0.001 gm.) of the drug are of service in *hemorrhoids*.

In operations on the eye, nose, throat, etc. the drug serves not only to control bleeding, but also to delay the absorption of cocain and to prolong local anesthesia. In cerebral, pulmonary and other internal hemorrhages constriction of the vessels by the intravenous injection of epinephrin is likely to prove harmful by raising the general bloodpressure.

Applications of epinephrin to the nasal mucous membrane sometimes afford temporary relief in *coryza* and *hay fever* by shrinking the inflamed tissues, although their secondary effect (vasodilation) is unfavorable. In the form of an ointment or of suppositories the drug is often of benefit in *anal pruritus*.

As the characteristic effects of epinephrin on the general circulation are observed only after intravenous or intramuscular injection, and even then are only momentary, it follows that the field of usefulness of the drug as a circulatory stimulant must be a limited one. It is chiefly indicated in marked vasodilation. Thus, in *shock* and *collapse* it may prove life-saving. In these conditions it should be given intravenously drop by drop, or better, by intravenous transfusion, using a very dilute solution (1:100,000). The injection must be given slowly, the effect being carefully noted, for if used too freely the drug is likely to cause cardiac dilatation, with pulmonary edema, especially if the heart muscle itself is seriously affected. It has been shown that this untoward result is likely to occur especially in chloroform poisoning, and that chloroform and epinephrin are each contraindicated when the other has been used.

In many cases of *bronchial asthma* epinephrin affords prompt relief. The good effects usually last at first two or three hours, but tolerance to the drug is gradually established and eventually it may prove ineffectual. The dose is from 5 to 15 minims (0.3–1.0 mil) of the 1:1000 solution, subcutaneously. At the very beginning of an attack 2 minims (0.1 mil) or even 1 minim (0.06 mil) may suffice.

Desiccated suprarenal glands (Suprarenalum Siccum, U. S. P.), in doses of from 10 to 20 grains (0.6–1.3 gm.), thrice daily, seems to have been of some value in *Addison's disease*. The good effects, however, have never been lasting. Subcutaneous

injections of epinephrin—15 minims (1.0 mil)—have also been used with some success in *osteomalacia*.

HYPOPHYSIS SICCA, U. S. P.

(Desiccated Hypophysis, Pituitary Extract)

Desiccated hypophysis is the posterior lobe of the pituitary body of cattle, cleaned, dried and powdered. The active constituents of the drug are soluble in water and are not destroyed by boiling, but their nature is unknown. The average dose is $\frac{1}{2}$ grain (0.03 gm.).

PREPARATION

DOSE

Liquor Hypophysis, U. S. P. 15 min. (1.0 mil)

Pharmacologic Action.—Circulatory System.—The effects of pituitary extract upon the circulation are somewhat similar to those of epinephrin, although they are produced in a different way. Administered intravenously, the drug causes a rise in arterial pressure, with some slowing of the pulse and weakening of the cardiac contractions. These effects are much less pronounced after intramuscular or subcutaneous injection and are not observed at all after administration by the mouth. With frequently repeated injections of large amounts the blood pressure rises less and less, and eventually it may actually fall. The increased blood pressure is of vascular origin, for it is accompanied by a shrinking in the volume of the viscera, and it is the result of a peripheral action, for it occurs after destruction of the central nervous system. When a solution of hypophysis is perfused through an excised organ the outflow is much decreased, and, moreover, this effect is not offset by ergotoxin, which paralyzes vasoconstrictor nerve-endings; therefore, it may be assumed that the drug does not stimulate the nerve-endings, like epinephrin, but the arterial muscle itself. The rise in arterial pressure is not quite so pronounced or so rapidly produced with pituitary extract as with epinephrin, but it is somewhat more sustained, usually lasting from fifteen minutes to half an hour. The slowing of the pulse is probably due to stimulation of the vagus center by the increased blood pressure and the weakening of the ventricular contractions, the effect of which is completely offset by the vasoconstriction, is apparently the result of direct cardiac depression.

Applied to mucous membranes and raw surfaces, solutions of hypophysis contract the arterioles, although less powerfully than solutions of epinephrin. The drug is without effect upon the unbroken skin.

Kidneys.—In the intact animal pituitary extract usually, but not invariably, increases somewhat the output of urine, probably by increasing the blood pressure within the capillaries of the glomeruli. At present this finding is irreconcilable with the clinical observation that injections of pituitary extract decidedly diminish urination in diabetes insipidus.

Intestines.—Subcutaneous injections stimulate the intestinal muscle, increasing tonus and peristalsis.

Mammary Gland.—In nursing animals intravenous or intramuscular injections of pituitary extract are followed almost immediately by an increase in the amount of milk, but this effect is very transitory, and at the next milking the secretion is correspondingly decreased both in quantity and quality. It is likely, therefore, that the drug does not actually increase lacteal secretion, but merely causes a more complete expression of accumulated milk by stimulating the smooth muscle of the gland.

Uterus.—Intravenous, intramuscular or subcutaneous injections have a pronounced stimulating affect upon the uterus, especially in pregnancy. In parturition the drug increases both the strength and rapidity of the contractions, although it does not usually cause tetanic constriction unless given in large doses. The site of its action is apparently the uterine muscle itself.

Muscles.—The dominant action of pituitary extract is on smooth muscle. It stimulates not only the muscle of the arteries, intestines, mammary glands, and uterus, but also that of the bronchi and urinary bladder.

Therapeutics.—The solution of hypophysis has been used somewhat extensively in *labor* to hasten delivery, but this use is not without danger and occasionally the drug fails to act. Instances of asphyxia of the fetus, rupture of the uterus, premature separation of the placenta, and laceration of the cervix or perineum have frequently been reported. As an oxytocic the drug should be employed only when the cervix is fully dilated and the delay in delivery is caused solely by uterine inertia. Any mechanical obstacle to natural delivery is a contraindication. The dose is $\frac{1}{2}$ c.c. ($\frac{1}{2}$ mil), intramuscularly, repeated in one hour, if necessary. In *postpartum hemorrhage* the action of pituitary extract is more prompt and powerful than that of ergot, but is less persistent. Its use should be supplemented with that of ergot. A dose of 1 c.c. (1 mil), intramuscularly, repeated in two hours, if necessary, is sometimes efficacious in *paralytic distention of the intestines*, resulting from acute infections, such as pneumonia, or following surgical operations. The drug is also of value in *postoperative anuria, the result of vesical atony*. As a vasoconstrictor the solution of pituitary extract (1 mil) is sometimes

given intramuscularly in conditions of *heart failure* with *low blood pressure*. Its action, while less rapid than that of epinephrin, is more sustained. It has also been recommended for combating the low blood pressure of *Addison's disease*.

Subcutaneous injections of an aqueous extract (1 mil once a day) often afford great relief in *diabetes insipidus*, although the effect of the drug rarely lasts more than twenty-four hours. Oral administration is ineffectual.

Administration.—For hypodermic injection solutions contained in sterile ampules should be used rather than the official preparation.

GLYCERYLIS NITRAS

(Nitroglycerin, Glyceryl Trinitrate, Glonoin, Trinitrin, $C_3H_5(NO_3)_3$)

Nitroglycerin is prepared by gradually adding dehydrated glycerin to nitric acid, or a mixture of nitric and sulphuric acids. It is official in the form of a 1 per cent. (by weight) alcoholic solution (*Spiritus Glycerilis Nitratis*, U. S. P.), the dose of which is from 1–3 minims (0.06–0.2 mil), cautiously increased until effects are manifested. The spirit should be kept in well-stoppered tin cans, and should be stored in a cool place, remote from lights or fire. Care must be exercised in handling it, since a dangerous explosion may occur if any considerable quantity be spilled.

Pharmacologic Action.—**Circulatory System.**—The administration of nitroglycerin (glyceryl trinitrate) or of a nitrite in quantities sufficient to produce its characteristic effects is speedily followed by flushing of the face and neck, a sense of fullness in the head, quickening of the pulse and a pronounced fall of blood pressure. After a large dose headache, dizziness and mental confusion may also be present. These symptoms are due to dilatation of the arterioles and depression of the vagus. The vasodilation, which is especially marked in the “blush area” of the skin and in the abdominal organs, is peripheral for it occurs after destruction of the spinal cord and in excised organs. As the drug dilates the coronary arteries, in which the existence of vasomotor nerve-fibers is doubtful, the site of its action is probably the arterial muscle itself. The quickening of the pulse appears to be due to depression of the vagus center, for after paralysis of the vagi by atropin the drug causes little or no additional increase in the rate. The depression of the vagus center is probably due to the fall of blood pressure and not the direct action of the drug on the center itself, for no acceleration of the pulse occurs if the general arterial pressure is maintained by compression of the aorta (Filehne, Sollmann).

The nitrites do not affect the heart directly, but by depressing the vagus and thus increasing the tonicity and contractility of the heart-muscle, by relaxing the coronary arteries and improving the myocardial circulation, and by lessening the resistance in the peripheral arteries they may sometimes afford relief in cardiac insufficiency.

The effect of nitroglycerin on the circulation, whether the drug is given by the mouth or subcutaneously, is produced within a few minutes, reaches its maximum in fifteen minutes, and lasts from one-half to two hours.

Blood.—When mixed with a nitrite blood acquires a chocolate color, owing to the transformation of oxyhemoglobin into methemoglobin. This compound is more stable than oxyhemoglobin, and cannot act as an oxygen carrier. In man the amount produced by therapeutic doses, however, is so small that no harmful effects are seen. The blood-cells themselves are not damaged, as with many other methemoglobin formers (coal-tar derivatives, potassium chlorate, pyrogallol), and in a short time the methemoglobin is reduced by the tissues and replaced by oxyhemoglobin. When present in the blood in large quantities methemoglobin gives rise to cyanosis and intense dyspnea.

Respiratory System.—Moderate doses slightly increase the rate and depth of the respirations, probably through their action on the circulation.

Nervous System.—The nitrites have no direct action on the nervous system. The ringing in the ears, headache, etc., which are observed after large doses, are the result of dilatation of the cerebral vessels. Convulsions sometimes occur in poisoning, but they are probably caused by circulatory changes.

Muscle.—Other forms of smooth muscle, such as that of the bronchioles, ureters and intestines, are also relaxed by the nitrites, although not to the same extent as that of the blood vessels.

Temperature.—Some fall of temperature occurs after moderate doses, as a result of dilatation of the cutaneous vessels and increased radiation of heat.

Excretion.—Nitroglycerin circulates in the blood largely as nitrites. These undergo oxidation, part being completely disintegrated and part appearing in the urine as nitrates.

Therapeutics.—Nitroglycerin is often useful in *chronic myocardial disease*, especially when there is precordial discomfort or paroxysmal breathlessness. In the minor degrees of the affection it is sometimes advantageous to give it with digitalis, the dose of each drug being carefully observed and regulated. The nitroglycerin having a prompt but fugacious action should be given two or three times as frequently as the digitalis, which

acts slowly but persistently. In acute myocardial disease the drug may do harm by lowering still further the arterial pressure, and in shock it is, of course, absolutely contraindicated.

In cases of *persistent high arterial pressure* nitroglycerin is often of service in relieving headache, precordial oppression, and asthmatic seizures, but it must always be used tentatively, especially if there is chronic nephritis, for if the blood pressure is too much reduced, increasing dyspnea, anuria and uremia may ensue. As a rule, better results are obtained in hyperpiesis of nephritic origin from rest, a diet low in protein food, and catharsis. When there is no serious myocardial disease, but the heart is in danger of being overborne by excessive labor digitalis is often more effective than nitroglycerin. In some cases of hyperpiesis, especially if there is edema, nitrites completely fail to lower the pressure.

In *angina pectoris* nitroglycerin, alone or in conjunction with potassium iodid, is often of great value in warding off the paroxysms. Its good effects are probably due to relaxation of the coronary arteries, and therefore, it may be employed even if the general blood pressure is not abnormally high. In the attacks of angina amyl nitrite acts a little more promptly, although nitroglycerin is usually efficacious. It may often be advantageously given with carminatives, such as spirit of chloroform and aromatic spirit of ammonia.

Small, frequently repeated doses of nitroglycerin are sometimes useful in controlling *persistent hiccough*. Wade recommends the drug in the *abdominal palpitations* frequently seen in nervous women. He believes that it acts by lowering the bloodpressure in the splanchnic area. Good results occasionally follow its use in *migraine*. Temporary relief is sometimes obtained from its use in the asphyxial stage of *Raynaud's disease*. It has also been recommended in *hemoptysis*.

According to M. Allen Starr, nitroglycerin, in doses of $\frac{1}{100}$ grain (0.00065 gm.) several times a day, combined with a heart stimulant, is of much more service in senile epilepsy or in epilepsy due to arteriosclerosis than the bromids.

Untoward Effects.—In certain individuals the smallest dose of nitroglycerin induces flushing of the face, headache, tinnitus aurium, and vertigo.

Administration.—Nitroglycerin acts almost as quickly when given by the mouth as when injected beneath the skin. The available preparations are the official spirit and the tablets, which are commonly found in the market, and which contain from $\frac{1}{500}$ to $\frac{1}{50}$ grain (0.0001–0.0012 gm.). It is very important that the preparation should be fresh, as both solution

and tablets deteriorate with age. On account of the extreme variation in individual susceptibility to the drug, small doses should be administered at first, and these gradually increased until the therapeutic or pharmacologic effect (flushing, etc.) is secured. According to Wood, a single drop has caused insensibility; on the other hand, Whittaker has given as much as $8\frac{4}{5}$ grains (0.56 gm.) in twenty-four hours without untoward effects. Tolerance is readily established, and this is another reason for making the initial doses the smallest that will prove effective.

AMYLIS NITRIS, U. S. P.

(Amyl Nitrite, $C_5H_{11}NO_2$)

Amyl nitrite is prepared by distilling equal volumes of pure amylic alcohol and nitric acid. It appears as a yellowish, highly volatile liquid having a strong ethereal odor.

Pharmacologic Action and Therapeutics.—Amyl nitrite produces the same effects as nitroglycerin, but when inhaled its action is more rapid, the fall in blood pressure beginning almost immediately, reaching its maximum within 2 or 3 minutes and disappearing within 10 minutes. Owing to its ephemeral effect it is not so useful in circulatory conditions associated with persistent high arterial pressure as nitroglycerin. In the seizures of *angina pectoris*, however, it is often very beneficial.

Inhalations of the drug are sometimes serviceable, too, in arresting the *convulsions of epilepsy*, *strychnin-poisoning* and *uremia*, although the manner of their action is not apparent. Inhalations may also prove efficacious in *asthma* and *whooping-cough*.

Administration.—Amyl nitrite is almost always given by inhalation: 2 to 5 minims (0.1–0.3 mil) may be dropped upon a handkerchief, or one of the small glass capsules ("pearls") containing the requisite dose may be crushed in a handkerchief, and the vapor inhaled. According to Osler, it sometimes acts better in *angina pectoris* when given by the mouth, combined with the tincture of capsicum and peppermint-water. As a rule, however, nitroglycerin is better suited for internal administration.

ERYTHROL TETRANITRATE

(Tetranitrol, $C_4H_6(NO_3)_4$)

Erythrol tetranitrate occurs in the form of large scales, which are soluble in alcohol, insoluble in water, and which readily explode on percussion. In the form of coated tablets, however, it may be handled with safety. The dose is from $\frac{1}{2}$ to 1 grain (0.03–0.06 gm.).

Pharmacologic Action and Therapeutics.—Erythrol tetranitrate acts similarly to nitroglycerin, but the fall of blood-pressure is produced more slowly and is more prolonged. The maximum effect is reached in about half an hour and the return of the pressure to normal occurs in from 3 to 4 hours. Patients vary considerably in their susceptibility to the drug, but tolerance is not so readily established as with nitroglycerin.

Erythrol tetranitrate is somewhat expensive for ordinary use, but it may be given in the same class of cases as the other members of the series.

SODII NITRIS, U. S. P.

(Sodium Nitrite, NaNO_2)

Sodium nitrite occurs in the form of white, opaque, fused masses, or colorless, transparent crystals, odorless, and of a mild saline taste. It is soluble in 1.4 parts of water, and sparingly soluble in alcohol. On exposure to air it deliquesces and is gradually oxidized to sodium nitrate, thereby losing its efficiency as a vasodilator. The dose is from 1–3 grains (0.06–0.2 gm.).

Pharmacologic Action and Therapeutics.—The effects of sodium nitrite are similar to those of nitroglycerin, except that they are produced more slowly and are more abiding. The fall of blood pressure begins within 15 minutes, reaches its maximum in half an hour and disappears in from 1 to 2 hours. Although sodium nitrite is less likely to cause headache than the organic nitrates, it not rarely causes more or less digestive disturbance by liberating nitrous acid in the stomach. It is indicated in the same class of cases as nitroglycerin and erythrol tetranitrate, but in general it is less reliable.

BENZYL BENZOATE

($\text{C}_{14}\text{H}_{12}\text{O}_2$)

Benzyl benzoate is an ester of benzyl alcohol and benzoic acid. It is present in certain aromatic balsams, such as balsam of Peru and balsam of Tolu, and can be made synthetically from benzaldehyd. It is a clear colorless liquid, almost odorless and of a pungent unpleasant taste. It is almost insoluble in water or glycerin, but is soluble in alcohol, ether or warm olive oil. The dose is from 15 to 30 minims (1.0–2.0 mls), dissolved in alcohol or aromatic elixir and diluted with milk or water, every 2 to 4 hours. It may also be prescribed in the form of a 20 per cent. aromatized emulsion, the dose of which is $\frac{1}{2}$ to 2 fluidrams (2.0–8.0 mls), well diluted with milk or water.

Pharmacologic Action and Therapeutics.—Benzyl benzoate has peripheral actions similar to those of the benzylisoquinolin group of opium alkaloids, exemplified by papaverin, but it is without the slight narcotic action of the latter. Applied directly or injected intravenously, it relaxes the tonus of all smooth muscle. The drug has little effect upon the heart, but lowers the blood pressure through a peripheral vasodilator action. Its toxicity is low. It is excreted largely in the urine as hippuric acid.

Clinically, benzyl benzoate has been used with some success to produce relaxation of smooth muscle in such conditions as *dysmenorrhea*, *intestinal colic*, *mucous colitis*, *pylorospasm*, *irritability of the bladder*, *asthma*, *whooping cough*, *hiccup*, *arterial hypertension*, etc. On the whole, however, the results have been much less favorable than were anticipated from the experiments of Macht, who introduced it into medicine, and probably because when administered by the mouth benzyl benzoate is soon conjugated in the body with glycocoll, and, therefore, rendered physiologically inactive. The unpleasant taste and after-taste of the drug and the burning sensation that it produces in the throat and epigastrium are objectionable features in all preparations.

RESPIRATORY STIMULANTS AND DEPRESSANTS

Respiratory Stimulants.—The following drugs stimulate the respiratory center in the medulla:

Caffein	Cocain
Atropin	Aspidospermin
Strychnin	Ammonia (reflexly).

In addition to these drugs, *external heat* increases the depth of the respirations. The expiratory and inspiratory fibers of the vagus are stimulated by the rhythmic expansion and collapse of the lung, which takes place in the practice of artificial respiration by *Sylvester's method*. In pursuing this method the patient is placed in a supine position; his arms are drawn upward and outward so as to fully expand the chest; after a pause of a few seconds the arms are brought down forcibly to the sides of the chest and pressed against them for a second. These movements are repeated about sixteen or eighteen times in a minute. The respiratory center may be stimulated also reflexly by irritating certain peripheral sensory nerves. Thus, in *Laborde's method* of treating asphyxia by rhythmic traction of the tongue, the center is affected through the sensory nerves of the

nervous excitability and insomnia; and that others still in large amounts cause not only in turn symptoms of increased and decreased psychic and motor activity, but sometimes even simultaneously some symptoms of stimulation and others of depression. The most important stimulants of the psychic functions are:

Caffein

Cocain.

Caffein is much the stronger stimulant of the two and even in large doses does not cause a later stage of pronounced depression, although it may produce more or less mental confusion. It has but little effect upon the motor functions of the brain, the convulsions that sometimes result from toxic doses being of spinal origin. With cocain the stage of psychic stimulation is short and is followed by one of profound depression, not unlike that produced by morphin. Moreover, while cocain is depressing the psychic functions it may be stimulating the motor centers from above downward, acute poisoning being marked not only by unconsciousness but also by convulsions, which at first may have their origin in the cerebral cortex, then in the hind brain, and at last in the spinal cord.

More typical, however, of combined stimulation and depression of the cerebral functions are the effects produced by

Atropin.

Ordinary therapeutic doses of this drug are without appreciable effect upon the cerebrum, but toxic doses produce a condition in which symptoms of motor and psychic stimulation and depression are variously combined. It is only in the final stages of atropin-poisoning that the cerebral paralysis is so complete that no evidences of stimulation are discernible.

Of the other alkaloids of the belladonna group, *hyoscyamin* acts like atropin, while *scopolamin* (*hyoscin*) is almost purely depressant to the cerebrum and causes little or no primary stimulation.

Alcohol, ether and a number of other drugs, in moderate doses, cause more or less mental excitement, but at no time exert any stimulant effect upon the higher intellectual functions—attention, perception, judgment, etc.—the excitement being apparently due to depression of the cerebral inhibitory or controlling centers.

Among the many drugs that are capable of causing epileptiform convulsions in toxic doses may be mentioned *santonin*, a neutral body from Levant wormseed, and certain *volatile oils*, such as camphor, oil of wormwood (absinth), oil of tansy, and oil of nutmeg. In some instances the poison acts on a subcortical

center rather than on the cortex of the cerebrum; thus, *picrotoxin*, a neutral principle from *Cocculus indicus* ("fish-berries"), in large doses, causes epileptiform convulsions which are apparently caused by intense stimulation of the medulla, since they persist after removal of the hemispheres and section below the optic thalami.

Indications.—A few of the cerebral excitants, especially atropin and caffein, are sometimes useful in arousing the cerebral centers when they have been profoundly depressed by narcotic poisons, such as opium.

BELLADONNA

(Deadly Nightshade)

Belladonna is official as the leaves (*Belladonna Folia*) and as the root (*Belladonna Radix*) of *Atropa Belladonna*, a bushy perennial, a native of Europe, but largely cultivated in North America. The chief active constituents are the two alkaloids *atropin* and *hyoscyamin*, though a third alkaloid, *scopolamin*, is also present in minute quantities. Hyoscyamin is isomeric with atropin and is readily converted into it by alkalis and a number of other agents. Indeed, the preparations of belladonna owe their activity mainly to atropin, which is official as *Atropina* and *Atropina Sulphas*. Atropin is also present in Stramonium, Hyoscyamus, Scopola, and other plants belonging to the order Solanaceæ,* although in hyoscyamus and scopola scopolamin (hyoscin) is the dominant alkaloid.

Both atropin and atropin sulphate appear as a white crystalline powder, having an acrid, bitter taste. The former is only slightly soluble in water, the latter in 0.4 part of water or 5 parts of alcohol. The dose of atropin and its salts is $\frac{1}{200}$ to $\frac{1}{75}$ grain (0.0003–0.00085 gm.).

PREPARATIONS

DOSE

Tinctura Belladonnæ Foliorum, U. S. P. 5–20 min. (0.3–1.2 mil)
 Extractum Belladonnæ Foliorum, U. S. P. . . . $\frac{1}{8}$ – $\frac{1}{4}$ gr. (0.008–0.016 gm.)
 Fluidextractum Belladonnæ Radicis, U. S. P. 1–3 min. (0.06–0.2 mil)
 Linimentum Belladonnæ, U. S. P. (fluidext. with 5 per cent. of camphor)
 Unguentum Belladonnæ, U. S. P. (10 per cent. of extract).

Pharmacologic Action.—Atropin stimulates and then depresses the cerebrum and certain medullary centers, depresses the peripheral distribution of the parasympathetic nerves of the autonomic system (see p. 177), and, when locally applied, slightly depresses the sensory nerve-endings.

* The ubiquitous nightshade family includes also the potato, the tomato, the horsetail, the tobacco, and the eggplant.

Circulatory System.—Atropin stimulates the vagus center in the medulla, but this effect is more than offset by depression of the vagus endings in the heart; large doses, therefore, increase the rate of the pulse. The drug also slightly raises the blood pressure, chiefly by quickening the output of the heart, but partly by stimulating the vasoconstrictor center. The vasoconstriction occurs principally in the splanchnic region, and the superficial vessels, especially those of the face, neck and chest ("blush area") are actually dilated. After large doses this effect on the cutaneous vessels is often so pronounced that it results in a diffuse erythematous rash. Toxic doses of atropin lower the bloodpressure by depressing both the vasomotor center and the heart muscle.

Respiratory System.—In large doses atropin is a respiratory stimulant, increasing the rate and depth of respiration. This effect is due partly to stimulation of the respiratory center, and partly to dilatation of the bronchi through depression of the vagus endings. Toxic doses depress the respiratory center and in fatal poisoning death is usually due to asphyxia.

Nervous System.—Therapeutic doses of atropin do not, as a rule, affect the *cerebrum*, but large doses have first a stimulating and then a depressing effect upon both the psychic and motor functions, producing in turn restlessness, mental exhilaration and talkativeness, delirium with hallucinations, and, finally, depression with stupor and coma. In the *medulla* the drug stimulates the respiratory center, and also slightly the vagus and vasomotor centers.

In man the action of atropin on the *spinal cord* is entirely overshadowed by its action on the cerebrum and medulla. In the frog, however, large doses increase reflex excitability and cause tetanic convulsions. Atropin depresses the endings of the *parasympathetic nerves* throughout the body, including the oculo-motor endings (mydriasis, etc.), the vagal endings in the heart, bronchi, and bowel (quickening of the pulse, relaxation of the bronchi, and suppression of colic), and the chorda tympani endings (dryness of mouth and throat). It also depresses the sympathetic endings in the sweat-glands, the innervation of the latter reacting to drugs as if it were parasympathetic. Finally, when locally applied, atropin slightly depresses the peripheral *sensory nerves*.

Eye.—Atropin dilates the pupil and paralyzes accommodation. The first effect (mydriasis) is due to depression of the oculo-motor endings in the sphincter muscle of the iris, which leaves the action of the radial or dilator muscle (sympathetic innervation) unopposed. The second effect (cycloplegia) is due to depression of the oculomotor endings in the ciliary muscle,

which results in flattening of the lens and, therefore, in adjustment of the focus only for distant objects. The occurrence of the mydriasis in an excised eye shows that it is of peripheral origin, and the contraction of the pupil of an atropinized eye upon direct stimulation of the iris but not upon stimulation of the oculomotor nerve trunk indicates that the site of the drug's paralyzing action must be in the endings of the oculomotor nerve. Although the ocular actions of atropin may be produced by administering the drug internally, they occur much more readily with its local application. After repeated applications to the eye the cycloplegia usually lasts about a week and the mydriasis about ten days.

Mydriasis resulting from atropinization of the eye is accompanied by more or less photophobia, slight analgesia of the cornea and iris, and an increase in the intraocular tension. The first of these effects is due to the unrestricted entrance of light; the second, to depression of the peripheral sensory nerves of the eye; and the last, to compression of the spaces of Fontana by the retraction of the iris and consequently interference with the escape of the aqueous humor.

Digestive Tract.—Atropin diminishes the total quantity of gastric juice and also the percentage of hydrochloric acid. It has apparently little effect on the bile or pancreatic secretion, although by lessening gastric acidity it may decrease the production of secretin in the bowel and thus possibly diminish indirectly to some extent the output of pancreatic juice. Large doses by depressing the vagus motor nerve-endings tend to overcome abnormal contractions of the gastric muscle, such as occur in reflex pylorospasm.

While the drug has little or no effect on normal intestinal peristalsis, which is largely under the control of Auerbach's plexus, it does tend to check abnormal tonic contractions of the bowel caused by overaction of the vagus, such as occur in spastic constipation or follow the use of irritant cathartics. By depressing the fibers of the vagus distributed to the bile-ducts it also serves to inhibit painful spasms (biliary colic) excited by irritation within in the gall-bladder or by the passage of gall-stones through the ducts.

Secretory Glands.—By depressing the nerve-endings in the secretory glands atropin diminishes the saliva, the mucous secretion of the respiratory passages and alimentary tract, the gastric juice and the sweat. Milk secretion and pancreatic secretion are less affected, as they are only partly dependent upon central innervation, and the urine and bile show no decrease. The action of atropin on secretion is opposed by that of pilocarpin.

Temperature.—Large doses of atropin often cause a marked rise of temperature, probably by suppressing the secretion of sweat, although it is possible that the drug may also have some action on the heat-controlling centers.

Elimination.—Atropin is excreted rapidly by the kidneys, the greater part being unchanged. A certain amount of the drug, however, is destroyed in the tissues.

Toxicology.—The characteristic phenomena of belladonna-poisoning are dryness of the throat with huskiness of the voice, difficulty in deglutition and thirst, dilatation of the pupils and impairment of vision, a rapid tense pulse, hurried respiration, restlessness with talkative delirium, diffuse redness of the skin, especially on the face, neck and chest, and, finally, stupor deepening into coma, shallow respiration, collapse and death from asphyxia. The lethal dose of atropin for an adult is about 2 grains (0.13 gm.).

The urine of patients suffering from belladonna-poisoning if dropped into the eye of a cat causes dilatation of the pupil.

Treatment.—The indications are to precipitate the alkaloid with tannin, to wash out the stomach, and to combat the symptoms. For the delirium an ice-cap may be applied to the head and bromids or possibly small doses of morphin administered. Pilocarpin and physostigmin are antagonistic to atropin in some respects, but as they may also depress the respiration they are probably better avoided. Respiratory failure and collapse will require the use of medullary stimulants, especially caffein, of artificial respiration and of intravenous injections of normal saline solution. Catheterization of the bladder is usually necessary owing to the retention of urine.

Therapeutics.—Atropin or belladonna is employed chiefly to overcome spasm of smooth muscle, to diminish secretion, to dilate the pupil and paralyze ocular accommodation, to check excessive stimulation of the cardiac branches of the vagus, to neutralize the effects of certain poisons, and to depress the sensory nerve-endings.

To Relax Spasm.—In severe attacks of *biliary*, *renal*, or *intestinal colic* atropin is a valuable adjuvant to morphin, and should be given freely not only to relax the painful spasm, but also to offset the depressant action of the morphin on the respiration. In *lead colic* it relaxes the bowel, and thus tends to relieve both the pain and constipation. As it diminishes the excitability of the vagus endings, it is also of value in *spastic constipation*, due to chronic appendicitis, ovaritis, cholecystitis, etc. Combined with cathartics it tends to eliminate *gripping* (tonic spasm) without opposing the stimulant effect of such drugs on peristalsis.

In the same way it is useful in *reflex cardiospasm* or *pylorospasm*. When *incontinence of urine* is due to abnormal vesical irritability, which is not rarely the case in childhood, belladonna is often of service. To insure full benefit, however, it must be pushed until the pharmacologic effect is produced, as shown by dryness of the throat and slight dilatation of the pupils.

Bronchial asthma is not rarely favorably influenced by atropin or belladonna, although epinephrin is usually more effective. Atropin in doses of $\frac{1}{200}$ to $\frac{1}{150}$ grain (0.0003–0.0004 gm.) often lessens the nasal secretion and relieves the oppression of breathing in *hay fever*. The drug is sometimes of service also in *whooping cough*, although the manner of its action in this disease is not altogether apparent. To be efficient, it should be given in increasing doses until slight flushing of the face or mydriasis results.

To Diminish Secretion.—Atropin is one of the reliable remedies for controlling the *night-sweats of tuberculosis*. A dose of $\frac{1}{200}$ to $\frac{1}{150}$ grain (0.0003–0.0004 gm.) at bedtime is usually sufficient. Unfortunately, side-effects, such as dryness of the throat and thirst, often impair its usefulness. In *hyperidrosis* of the hands and feet it is recommended both as an internal remedy and as a local application. In *salivation* from overdoses of mercury it is also useful. When the mother is unable to suckle her infant and the breasts in consequence become swollen and tender the thorough application of the ointment of belladonna may serve to diminish the secretion of milk and avert suppuration even though this seems imminent. In *hyperchlorhydria* belladonna in full doses serves to lessen the secretion of acid and also to inhibit the tonic spasms of the stomach upon which the pain in this condition probably depends. In *bronchopneumonia* occurring in childhood belladonna in comparatively large doses (2 drops of the tincture every hour) is often of value in lessening the excessive secretion formed in the bronchi. As a *preliminary to general anesthesia* atropin, $\frac{1}{150}$ grain (0.0004 gm.), is sometimes used not only to lessen the danger of respiratory depression, but also to diminish salivation and bronchorrhea. In *coryza* with profuse secretion atropin or belladonna, in small doses, is a useful adjuvant to other remedies.

To Dilate the Pupil and Paralyze Ocular Accommodation.—Atropin may be employed as a mydriatic to *facilitate ophthalmoscopic examination*, but euphthalmin, cocain, or homatropin should be given the preference, as the action of these drugs is much less persistent. In *estimating errors of refraction* it is necessary to select a mydriatic that will suspend accommodation, and for this purpose atropin is often used, although homatropin

has the advantage of being less persistent in its action, while equally effective as a cycloplegic. In *iritis* atropin is indispensable in securing rest for the iris, in relieving pain, and in preventing adhesions to the lens or cornea, or in breaking up adhesions that have recently been formed. In *acute keratitis* it is also very useful in allaying ciliary irritation.

To Check Excessive Stimulation of the Cardiac Branches of the Vagus.—Atropin is of service in preventing *sudden arrest of the heart* through excessive vagus stimulation during the induction of anesthesia by chloroform. *Cardiac irregularity* and *partial heart-block of vagus origin* may also be lessened in degree or abolished by hypodermic injections of atropin. In complete heart-block the drug is of no avail.

To Neutralize the Effect of Certain Poisons.—By counteracting cerebral and respiratory depression, atropin is a useful antidote in *poisoning by chloral, morphin, and other narcotic drugs*. It is also of great value in overcoming the bronchial spasm, bronchorrhoea and respiratory depression resulting from *overdoses of pilocarpin*. Atropin is the best antidote in poisoning by the fly agaric, *Amanita muscaria*, and other mushrooms containing *muscarin*, the effects of which closely resemble those of pilocarpin. It is of no value, however, in antagonizing the toxin of the death's head fungus, *Amanita phalloides*, to which most cases of mushroom poisoning are due. By overcoming the tetanic contraction of the bronchial muscles, the drug may relieve the respiratory embarrassment of *anaphylactic shock*.

To Depress the Sensory Nerve-endings.—Internally, belladonna is a useful sedative in *acute cystitis* and *urethritis*. Locally, in ointment or suppository, it sometimes relieves the pain of *hemorrhoids* and of *anal fissure*. An ointment of belladonna and mercury has been much used for its sedative and absorbent properties in *orchitis* and *simple non-suppurative adenitis*.

Administration.—The root and leaves are not used internally. The tincture is a reliable liquid preparation. Children are relatively less susceptible to belladonna than adults, and, therefore, often tolerate much larger doses than their age would apparently indicate.

For instillation into the eye and subcutaneous injection the sulphate of atropin, on account of its ready solubility in water, is the alkaloidal salt almost always selected. As a simple mydriatic $\frac{1}{4}$ grain (0.016 gm.) to the ounce (30.0 mils) is usually sufficient, and the mydriasis from a solution of this strength will not last more than four or five days. As a cycloplegic to be used before examination for errors of refraction a strength of 4 grains (0.26 gm.) to the ounce (30.0 mils) should be

employed. A solution of the same strength is usually employed in iritis. In keratitis a solution of 1 to 2 grains (0.065–0.13 mg.) to the ounce (30.0 mils) is sufficiently strong. The following formulæ will illustrate the manner of prescribing the drug:

R̄. Atropinæ sulphatis..... gr. j (0.065 gm.)
 Acidi borici..... gr. x (0.65 gm.)
 Aquæ destillatæ..... f ʒj (30.0 mils).—M.
 Sig.—A drop or two to be instilled into the conjunctiva twice a day.
 (*Acute keratitis.*)

R̄. Tincturæ belladonnæ..... f ʒiss (5.5 mils)
 Glycerini..... f ʒij (8.0 mils)
 Aquæ menthæ piperitæ... q. s. ad f ʒij (60.0 mils).—M.
 Sig.—Thirty minims three times a day for a child of three years.
 The dose to be gradually increased until slight flushing of the face is induced. (*Whooping cough.*)

R̄. Extracti belladonnæ..... gr. iss (0.1 gm.)
 Codeinæ sulphatis..... gr. iiss (0.16 gm.)
 Pulveris camphoræ..... gr. xx (1.3 gm.)
 Ammonii carbonatis..... ʒi (4.0 gm.).—M.
 Pone in capsulas No. xx.
 Sig.—One every two hours. (*Acute rhinitis.*)

R̄. Extracti belladonnæ..... gr. x (0.65 gm.)
 Acidi tannici..... gr. x (0.65 gm.)
 Hydrargyri chloridi mitis..... gr. xxx (2.0 gm.)
 Phenolis..... gr. xx (1.3 gm.)
 Unguenti petrolati..... ʒj (30.0 gm.).—M.
 Sig.—Apply night and morning after washing the parts. (*Hemorrhoids.*)

Incompatibles.—Atropin should not be prescribed in solutions containing caustic alkalis or tannic acid.

STRAMONIUM

(Jamestown Weed, Thorn-apple)

The drug is official as the leaves of *Datura Stramonium*, a weed growing in waste places in Europe, Asia, and America. It contains *atropin*, *hyoscyamin*, and a minute quantity of *scopolamin*.

PREPARATIONS

DOSE

Tinctura Stramonii, U. S. P..... 5–20 min. (0.3–1.3)
 Extractum Stramonii, U. S. P..... $\frac{1}{8}$ – $\frac{1}{4}$ gr. (0.008–0.016 gm.)
 Unguentum Stramonii, U. S. P., contains 10 per cent. of the extract.

Therapeutics.—Stramonium has actions similar to those of belladonna, and may be used for the same purposes. It has a special reputation in *asthma*, in which disease the smoke of burning stramonium leaves may be inhaled. Ointment of stramonium with an equal amount of ointment of galls is a popular remedy for *hemorrhoids*.

HYOSCYAMUS, U. S. P.

Hyoscyamus is official as the leaves and flowering tops of *Hyoscyamus niger*, a plant growing in Europe, Asia and North America. It contains scopolamin (hyoscin) with smaller amounts of hyoscyamin and atropin.

PREPARATIONS	DOSE
Tinctura Hyoscyami, U. S. P.	20–40 min. (1.2–2.5 mils)
Fluidextractum Hyoscyami, U. S. P.	3–5 min. (0.2–0.3 mils)
Extractum Hyoscyami, U. S. P.	$\frac{1}{2}$ –2 gr. (0.03–0.13 gm.)

Pharmacologic Action.—The action of hyoscyamus resembles that of belladonna, but the official preparations are weaker.

HYOSCYAMINA

Hyoscyamin is an isomer of atropin, the latter being a loose combination of hyoscyamin and dextro-hyoscyamin (Cushny). It is official as *Hyoscyaminæ Hydrobromidum*, the dose of which is $\frac{1}{200}$ to $\frac{1}{150}$ grain (0.0003–0.0004 gm.).

Hyoscyamin has an action similar to that of atropin, but it depresses much more powerfully than the latter the parasympathetic nerve-endings in the sphincter muscle of the iris, in the smooth muscles of the viscera, in the secretory glands, etc. From a therapeutic view-point it has no advantages over atropin.

SCOPOLAMINA

Scopolamin, also known as hyoscin, is an alkaloid closely related to atropin and occurring with the latter in belladonna, stramonium, hyoscyamus, scopolia, and other plants of the Solanaceæ (potato family). It is official in the form of the hydrobromid (*Scopolaminæ Hydrobromidum*), the dose of which is $\frac{1}{200}$ to $\frac{1}{100}$ grain (0.0003–0.0006 gm.).

Scopolamin depresses the terminations of the same nerves as atropin. Its action in this respect, however, is more prompt and more powerful than that of atropin, and its effect somewhat less persistent. Unlike atropin, it depresses the cerebrum almost from the beginning, a dose of $\frac{1}{120}$ grain (0.0005 gm.) usually sufficing to induce sleep without giving rise to any preliminary stage of excitement. It also differs from atropin in not stimulating, but rather depressing, the respiratory and vasoconstrictor centers in the medulla. In a number of cases serious and even fatal collapse has followed its use. Toxic doses of the drug cause dilatation of the pupils, dryness of the throat, coma and collapse.

Therapeutics.—Scopolamin is used as a somnifacient, a depressomotor, an anaphrodisiac and a general anesthetic. It

is often an efficient somnifacient in *insomnia* associated with great mental and physical excitement, such as occurs in *acute mania*, *delirium tremens*, *melancholia agitata* and *drug addictions*. As it ordinarily has little effect on the circulation, it is sometimes of service in insomnia occurring in *chronic heart disease*, but usually it is inferior to morphin. Subcutaneously, in doses of $\frac{1}{200}$ grain (0.0003 gm.), twice daily, it may prove efficacious in the more severe forms of *acute chorea*. In *paralysis agitans* doses of $\frac{1}{200}$ grain (0.0003 gm.) by the mouth somewhat lessen the tremor, at least for a time. The drug is often a useful remedy in *spermatorrhea*, *erotomania* and allied sexual disturbances.

Scopolamin is also used to some extent as a *preliminary to anesthesia* and as an *anesthetic* itself. As a preliminary to general anesthesia, $\frac{1}{150}$ grain (0.0004 gm.) is given subcutaneously with $\frac{1}{4}$ grain (0.016 gm.) of morphin half an hour before the administration of the ether or chloroform. Employed in this way the drug increases the narcotic effect of the morphin and lessens to some extent the unpleasant features of the first stage of the anesthesia, but as it also increases considerably the danger of respiratory depression it is better avoided.

General anesthesia may be produced by the use of scopolamin and morphin alone. For this purpose $\frac{1}{160}$ grain (0.0004 gm.) of scopolamin and $\frac{1}{6}$ grain (0.01 gm.) of morphin are injected subcutaneously two and one-half hours, one and a half hours, and one hour before the operation. The anesthesia, however, is not always complete, and inhalations of ether must sometimes be used in addition; moreover, serious accidents from scopolamin anesthesia have been by no means uncommon.

Partial scopolamin-morphin anesthesia has been used especially in *obstetrics*, the object being not so much to abolish the pains of labor as to make the patient forget them. The condition, which is really one of drowsiness with amnesia, has been described as "twilight sleep." The treatment is not begun until active labor pains have appeared, and then $\frac{1}{130}$ grain (0.00045 gm.) of scopolamin hydrobromid and $\frac{1}{8}$ to $\frac{1}{4}$ grain (0.008–0.015 gm.) of morphin sulphate are injected subcutaneously. The morphin is not repeated, but the scopolamin is given again in three-quarters of an hour, and then in somewhat smaller doses every one and one-half hours until the patient no longer remembers having seen objects that have been shown to her one-half hour before. The method is not always successful or safe for the mother and is distinctly dangerous to the child, and for these reasons it has been largely abandoned. It should never be attempted except in hospitals, where constant supervision of the patient is possible.

OTHER CEREBRAL EXCITANTS

Cocain (see p. 162).—This drug increases the activity of the cerebrum, small doses stimulating the psychic functions and somewhat larger doses the motor functions. As a motor stimulant it surpasses both atropin and caffein; as a psychic stimulant it is superior to atropin, but much inferior to caffein. The action of cocain as a local anesthetic is so much more important than that as cerebral excitant, that the drug is fully considered under Sensory Nerve Depressants (see p. 161).

CEREBRAL DEPRESSANTS

The cerebral depressants or narcotics may be classified as somnifacients, general anesthetics, general analgesics, anti-convulsants, and intoxicants.

SOMNIFACIENTS OR HYPNOTICS are remedies that produce sleep. The factors favoring natural sleep are the withdrawal of afferent stimuli, decreased responsiveness of the brain-cells as the result of fatigue, the accumulation in the blood of products evolved by the cells in the exercise of their functions, and, finally, lessening of the blood-supply to the brain. Pure somnifacients inhibit the functional activity of the brain-cells, but they do not completely suspend the power of the cells to recuperate (the main object of sleep) nor to react to stimuli which reach them from without.

Many theories have been advanced to explain the effect of narcotic drugs. According to the theory of *Meyer and Overton*, the aliphatic compounds or hydrocarbons (chloral, chloroform, paraldehyd, etc.), at least, owe their power to produce sleep and general anesthesia to their "solution affinity" for the lipoids or fatty substances, which are so abundant in the cells of the central nervous system. Owing to their fat-solvent action, these compounds readily enter the protoplasm of the cerebral cells, liquefy the lipoids, and thus directly alter the functions of the cells. Solubility in water is not without influence, as it is essential to absorption, and Meyer and Overton point out that the narcotic action of any of the aliphatic compounds is closely related to its "partition coefficient," that is, its solubility in fat divided by its solubility in water $\frac{S_F}{S_W}$. The higher this coefficient

the greater is the narcotic power. This theory, while it has much evidence to support it, does not explain the action of all narcotics. Morphin, scopolamin, bromids, etc. apparently act in an entirely different way.

Moore and Roaf believe that the lipid solubility is merely a

necessary condition for access to cell protoplasm by the narcotic, and that the action of the latter is chemical rather than physical. They suggest that narcosis depends upon the formation of a loose chemical combination between a portion of the drug and the protein of the cerebral cells, and that the portion of the drug which is taken up by the lipoids of the cells plays an entirely passive part.

Verworn, after drawing attention to the facts that narcosis is usually accompanied by diminished oxidation and that asphyxia produces an anesthetic effect, suggests that the lipoids may be carriers of oxygen and that narcotics may act by interfering with this function. This theory does not seem tenable, however, since anesthesia does not always diminish oxidation and since certain animal forms (intestinal parasites) are subject to narcosis by chloroform and yet can be kept alive in unoxygenated fluids.

The efficiency of the aliphatic narcotics may be modified by introducing into them certain other atoms or groups. Thus, it may be increased by the introduction of Cl or of O into the compound and decreased by the introduction of an acid or of more than one OH group.

GENERAL ANESTHETICS are drugs which acting on the central nervous system in concentrated form rapidly produce unconsciousness and insensibility. Their effect upon the brain-cells is more profound than that of the somnifacients in ordinary doses, for they temporarily inhibit the responsiveness of the cells to all external stimuli and suspend more or less completely recuperative changes. In large doses they depress also the motor functions of the spinal cord and the medullary centers.

GENERAL ANALGESICS OR ANODYNES are remedies that relieve pain without necessarily inducing unconsciousness or general anesthesia. They produce this effect directly through a selective depressant action on the sensory functions of the central nervous system. The most powerful analgesic is *opium*. It is capable of relieving pain without producing sleep or even without blunting ordinary sensory perception. While it has the power of relieving pain from almost any cause, it is especially useful in overcoming that resulting from gross lesions—inflammation, traumatism, and morbid growths. In so-called functional pains, such as headache, neuralgia, myalgia, etc., the coal-tar derivatives—*antipyrin*, *acetphenetidin*, *acetanilid*, *salicylates*—are more serviceable and less likely to produce a dangerous habit. The manner in which these drugs act is not definitely known, although it is probable that, like morphin, they directly depress the algesic centers. *Quinin* has a central analgesic action similar to that of the coal-tar derivatives, but it is very much less powerful.

Cannabis indica somewhat resembles opium in its analgesic action, but it is much less powerful. It has been especially recommended in migraine. The *bromids*, by depressing the cerebral cortex, often afford relief in headache, but in other forms of pain they usually fail.

ANTICONSULSANTS.—Certain drugs have the power of controlling epileptiform convulsions by directly decreasing the excitability of the motor centers in the brain. A drug that thus depresses the motor centers, and also lessens the power of the motor tracts of the spinal cord to convey discharges from the brain to the muscles, or lessens the power of sensory tracts of the spinal cord to transmit to the brain stimuli from without, has additional value as an anticonvulsant.

General anesthetics (ether and chloroform) profoundly affect the brain and the spinal cord, first depressing the sensory functions and then the motor. They are especially useful in controlling temporarily severe convulsive paroxysms, such as occur in the status epilepticus and in puerperal eclampsia. *Bromids* also depress the cerebrum and the spinal cord, and while their action is much less powerful than that of the anesthetics, it is much more persistent. They are especially valuable in idiopathic epilepsy and in the reflex convulsions of childhood, as they are but feebly depressant to the circulation and respiration. In many cases of epilepsy *phenobarbital* (*luminal*) proves even more satisfactory than the bromids.

Chloral is a more powerful depressant to the motor functions of the brain and cord than the bromids, but it is also more depressant to the circulation and respiration; moreover, it is much more likely to lead to habit formation than the bromids. It is, therefore, not suitable for frequent administration, but it may often be used with advantage in acute convulsive conditions, such as occur in eclampsia, tetanus, strychnin-poisoning, etc.

Antipyrin apparently depresses the motor functions of the brain as well as the sensory, and for this reason, probably, it is sometimes of service in reinforcing the action of the bromids in epilepsy. Its use must be limited, however, to short periods.

Amyl nitrite is often of value in aborting epileptic attacks, when these are preceded by a definite aura, but the manner of its action is not apparent.

INTOXICANTS.—Ethyl alcohol and methyl alcohol (wood alcohol) produce narcotic effects similar in kind to those of ether, but being less volatile, act more slowly and more persistently. As a narcotic, ethyl alcohol is sometimes efficacious in promoting sleep in mild forms of insomnia and in blunting perceptions and allaying nervous excitability in acute infections. Methyl

alcohol is valueless as a medicine, but it is important owing to the great number of cases of poisoning resulting from its use as a substitute for ethyl alcohol.

SOMNIFACIENTS

The treatment of insomnia is, of course, that of underlying condition. A potent factor in many of the more persistent forms is some disturbance of digestion or assimilation, and when this is the case a careful regulation of the diet is of the utmost importance. The evening meal especially should be light. Systematic exercise, preferably in the open air, and the occasional use of a mild mercurial or saline aperient are usually valuable aids. Tea, coffee, and tobacco are sometimes preventives of sleep, and if so, they must be used sparingly or altogether avoided. Insomnia from overwork, mental anxiety or grief will require mental rest, diversion, or change of scene. When anemia is a causal factor iron and arsenic are indicated. In chronic valvular disease with myocardial insufficiency digitalis is often more effective in promoting sleep than direct somnifacients. The insomnia of chronic nephritis may yield to a diet poor in proteins, to the use of eliminants, and, if the arterial tension is excessive, to the administration at night of a vasodilator, such as nitroglycerin. In the aged sleeplessness is sometimes associated with a lowered vascular tone, and if such is the case, small doses of strychnin are likely to be beneficial.

When the habit of sleeplessness has become well established it may require more than the removal of the cause to effect a complete cure. Simple measures, however, should always be tried first before resorting to somnifacient remedies. The bedroom should be quiet, well ventilated, and of moderate temperature. When the feet are cold the blood should be diverted from the head by hot foot-baths, which may be made more effective by the addition of mustard. Vigorous rubbing of the limbs is also useful. A glass of hot milk, a cup of bouillon, or a toddy just before retiring often acts favorably as a derivative. In some persons light reading for half an hour, in others a brisk walk, will invite sleep. In neurasthenia, massage and the systematic use of the wet-pack are often valuable aids.

Somnifacients must always be cautiously used. Their continued exhibition predisposes to invalidism and favors the development of vicious habits. In simple habitual insomnia they should not be prescribed until general measures have been tried and found wanting.

The chief somnifacients are:

Vegetable Group	Aliphatic or Hydrocarbon Group
Opium (morphin, codein)	Hydrated chloral } Aldehyds
Scopolamin or hyoscine	Paraldehyd }
	Sulphonal } Ethyl-sulphones
	Trional }
	Diethyl-barbituric acid (veronal) }
	Phenylethyl-barbituric acid (luminal) } Urea derivatives
	Ethyl carbamate }
Saline Group	
Potassium bromid	
Sodium bromid	
Strontium bromid	

OPIUM, U. S. P.

Opium is the inspissated juice* of the unripe seed-capsules of *Papaver somniferum*, a poppy growing in Western Asia. To be up to the official standard it should contain not less than 9 per cent. of morphin. It appears in the form of irregular lumps, having a dark-brown color, a gummy consistence, a strong peculiar odor, and a bitter taste. It contains *meconic acid* and, in addition to *morphin*, a number of other alkaloids, the most important of which are *codein* (0.2 to 0.7 per cent.), *papaverin*, *narcotin*, *narcein*, and *thebain*. Neither narcein nor thebain is used medicinally.

PREPARATIONS	DOSE
Opium, U. S. P. (9 per cent. of morphin.) . . .	½-2 gr. (0.03-0.13 gm.)
Opii Pulvis, U. S. P. (10-10.5 per cent. of morphin)	½-2 gr. (0.03-0.13 gm.)
Opium Deodoratum, U. S. P. (10-10.5 per cent. of morphin)	½-2 gr. (0.03-0.13 gm.)
Opium Granulatum, U. S. P. (10-10.5 per cent. of morphin)	½-2 gr. (0.03-0.13 gm.)
Extractum Opii, U. S. P. (20 per cent. of morphin)	¼-1 gr. (0.016-0.06 gm.)
Tinctura Opii, U. S. P. (laudanum; † 10 per cent. of granulated opium or 1 per cent. of morphin)	5-20 min. (0.3-1.3 mils)
Tinctura Opii Deodorati, U. S. P. (10 per cent. of granulated opium or 1 per cent. of morphin)	5-20 min. (0.3-1.3 mils)

* The name opium is from *ὀπός*, juice.

† The name "laudanum" is attributed to Paracelsus (1490-1541), but its origin is obscure. It is supposed by some philologists to be derived from the Latin *laudandum*, something to be praised, and by others to be a corruption of *vanodynum*, or the anodyne.

- Tinctura Opii Camphorata*, U. S. P. (paregoric;* 0.4 per cent. each of powdered opium, benzoic acid, camphor and oil of anise. One dram (4 mils) contains $\frac{1}{4}$ gr. (0.015 gm.) of opium..... 1-2 dr. (4.0-8.0 mils)
- Pulvis Ipecacuanhæ et Opii*, U. S. P. (Dover's powder†) contains 10 per cent. each of powdered opium and ipecac with sugar of milk) 5-10 gr. (0.3-0.6 gm.)
- Lotio Plumbi et Opii* (lead-water and laudanum; lead acetate, 4.5 gm., tincture of opium 9 mils, and water, q. s., 250 mils).

Morphin is the chief alkaloid of opium, and represents, in the main, its pharmacologic activity. It occurs in white prismatic crystals, in fine needles, or as a crystalline powder, sparingly soluble in water and of a bitter taste. The salts of morphin, being much more soluble than the alkaloid itself, are usually prescribed.

The following alkaloidal preparations are in use:

PREPARATIONS	DOSE
<i>Morphina</i> , U. S. P.....	$\frac{1}{8}$ - $\frac{1}{2}$ gr. (0.008-0.03 gm.)
<i>Morphinæ Hydrochloridum</i> , U. S. P.....	$\frac{1}{8}$ - $\frac{1}{2}$ gr. (0.008-0.03 gm.)
<i>Morphinæ Sulphas</i> , U. S. P.....	$\frac{1}{8}$ - $\frac{1}{2}$ gr. (0.008-0.03 gm.)
<i>Codeina</i> , U. S. P.....	$\frac{1}{4}$ -1 gr. (0.016-0.065 gm.)
<i>Codeinæ Phosphas</i> , U. S. P.....	$\frac{1}{4}$ -1 gr. (0.016-0.065 gm.)
<i>Codeinæ Sulphas</i> , U. S. P.....	$\frac{1}{4}$ -1 gr. (0.016-0.065 gm.)
<i>Papaverinæ Sulphas</i>	$\frac{1}{2}$ -2 gr. (0.03-0.13 gm.)
<i>Pantopon</i> (a mixture of the alkaloids of opium in their natural proportions).....	$\frac{1}{4}$ - $\frac{1}{2}$ gr. (0.016-0.03 gm.)
<i>Narcophin</i> (morphin-narcotin meconate; 33 per cent. of morphin).....	$\frac{1}{4}$ - $\frac{1}{2}$ gr. (0.016-0.03 gm.)

The following artificial derivatives of opium alkaloids are also in use:

Apomorphinæ Hydrochloridum, U. S. P. (Dehydrated morphin. See p. 184.)

Diacetylmorphinæ Hydrochloridum, U. S. P. (Heroin hydrochlorid. See p. 97.)

Æthylmorphinæ Hydrochloridum, U. S. P. (Dionin. See p. 97.)

Cotarninæ Hydrochloridum, U. S. P. (Stypticin. Prepared from narcotin. See p. 382.)

Apocodeinæ Hydrochloridum. (Dehydrated codein. See p. 294.)

Pharmacologic Action.—Nervous System.—In man the dominant action of opium is on the cerebrum. Even in comparatively small doses it dulls the perceptions, especially that of pain,

* The word "paregoric" is from the Greek *παρηγορικός*, which means soothing. The original formula was devised by Le Mort, a chemist at the University of Leyden (1702 to 1718).

† The formula of Dover's powder originated with Thomas Dover, a physician and adventurer, who lived in London in the latter part of the seventeenth century.

and causes drowsiness. Depression of the pain-perceiving (algesic) centers occurs long before the sensorium as a whole is affected. In full therapeutic doses the drug produces natural sleep, from which the patient usually awakes refreshed, but not rarely complaining of dull headache and nausea. Toxic doses are followed by profound coma. In some instances the narcotic effect is preceded by a short period of exaltation or exhilaration, with increased play of the imagination. This effect, as in the case of alcohol, is due to depression of the controlling centers rather than direct stimulation of the psychic functions. Unlike chloral, opium has little action, except in large doses, on the motor cells of the brain cortex.

Opium increases to some extent the reflex irritability of the spinal cord. In human beings this action is rarely apparent, owing to the much greater sensitiveness of the brain to the influence of the drug, but in animals, like the frog, in which the cerebral hemispheres are poorly developed, large doses give rise to tetanic convulsions. In some of the opium alkaloids, particularly thebain, the convulsant action is predominant.

In the medulla, opium decreases the excitability of the respiratory and cough centers, but with large doses it increases the sensitiveness of the vagus, the vomiting and the pupillo-constrictor centers. Its action on the vasomotor centers has not been definitely determined, although large doses undoubtedly depress the vasoconstrictor center, causing dilatation of the cutaneous vessels.

On the peripheral nerves opium has no effect, its value as an analgesic depending entirely upon its central action.

Respiratory System.—Opium is a powerful depressant of the respiratory center. In poisoning the respirations become progressively less rapid and more shallow, and, if the dose has been sufficiently large, finally cease entirely. With small doses there may be some increase in the depth of the respirations to compensate for the decrease in rate.

Circulatory System.—In full therapeutic doses opium dilates the cutaneous vessels and causes flushing, sweating, and occasionally itching; otherwise it has little effect on the circulation. In poisoning the pulse at first is full and somewhat infrequent from stimulation of the vagus center, and later it is feeble and frequent, as a result of asphyxia and of depression of the vasoconstrictor center.

Alimentary Canal.—The nausea and vomiting that not rarely occur after the administration of opium are of central origin. However, large doses tend to allay vomiting, probably by depressing the vomiting center. Even in small doses the

drug impairs the appetite, partly by lessening the perception of hunger and partly by disturbing digestion. Opium tends to excite the secretion of gastric juice, especially if administered when the stomach is empty. In morphinism, however, the gastric secretion is said to be diminished. The drug strongly depresses gastric motility and also prolongs the contraction of the gastric sphincters, especially the pyloric, and in consequence greatly retards the passage of the chyme into the intestine.

Even in small therapeutic doses opium tends to diminish intestinal peristalsis, to slacken the fecal current, especially in the upper bowel, and to cause constipation. These effects are due to several factors: (1) the slower passage of food into the intestine and its more complete maceration, as a result of the persistent closure of the pylorus; (2) diminished excitability of the defecation-reflex; and probably (3) depression of the nerve centers (Auerbach's plexus) in the intestinal wall. In certain animals large doses of morphin increase peristalsis and cause diarrhea, probably by directly irritating the bowel itself.

Urinary System.—Opium has little or no effect on the secretion of urine. In poisoning, however, it may cause retention of urine by producing spasm of the vesical sphincter. Reducing substances, usually morphin-glycuronic acid, but occasionally glucose, may appear in the urine after large doses of the drug.

Eye.—Applied to the conjunctiva, morphin has no effect upon the pupil, but when administered internally in toxic doses it causes extreme miosis through a central action. In fatal poisoning, dilatation of the pupil is observed just before death as a result of the asphyxia.

Secretions.—Opium decreases the saliva and the mucous secretions generally, probably by depressing the secretory centers. Under favorable conditions it increases the sweat by dilating the cutaneous vessels. It may also increase the gastric secretion.

Metabolism.—By lessening muscular activity and depressing respiration opium decreases the output of CO_2 and of urinary nitrogen. In poisoning it lowers the temperature by decreasing heat production (muscular inactivity) and by increasing heat dissipation (peripheral vasodilation).

Absorption and Elimination.—Morphin is rapidly absorbed from mucous membranes and raw surfaces, but very slowly and imperfectly from the unbroken skin. It escapes from the body chiefly through the stomach and bowel, only minute quantities appearing in the urine, saliva and milk. Elimination is rapid, and even after hypodermic injection the drug may be found in the stomach within a few minutes. Part of the morphin that is excreted in the stomach and bowel is reabsorbed. Ordinarily

only a small amount of the drug is destroyed in the tissues, but under increasing doses the proportion is gradually increased, so that in habitués only traces may appear in the excreta.

Conditions Modifying the Action of Opium.—Certain symptoms counteract the narcotic effect of opium, and when these are present the drug may be used in much larger doses than are usually prescribed; thus, patients suffering from affections attended with severe pain, such as acute peritonitis, renal or biliary colic, can frequently take with benefit doses that under other circumstances would produce profound narcosis. On the other hand, when there are evidences of nephritis the drug must be used with caution, since small doses not infrequently produce untoward effects.

Age and sex modify its action. Children, on account of the sensitiveness of their nervous systems, are peculiarly susceptible to opium, so that it must be given in smaller doses than the age would ordinarily indicate. A minim of laudanum is said to have produced a fatal result in a child less than six months old. Its action is more pronounced on women than on men, and in the former it is more likely to cause disagreeable after-effects.

Patients rapidly acquire a tolerance of the drug through frequent repetition of the dose, so that habitués can often take enormous amounts without experiencing the usual effects.

The Action of Opium and Morphin Compared.—Apart from being more powerful than opium, morphin differs from the latter in having a less constipating, less nauseating, and less diaphoretic effect.

Toxicology.—Acute Opium-poisoning.—Unless the dose is very large, there may be at first a stage of mild exhilaration, in which the imagination is stimulated and the feelings are exalted. This stage is soon followed by one of depression, in which the patient becomes listless and drowsy, and finally falls into a deep sleep. The pulse is slow and full, the pupils are contracted to a pin-point size, the respirations are slow and labored, the muscles are relaxed, and the face is pale. In this stage it is still possible to arouse the patient by loud noises, flagellation, or shaking. In the third stage coma is absolute, the pulse is rapid and irregular, the skin is clammy, and the breathing is shallow and irregular, and often of the Cheyne-Stokes type. Finally, death results from paralytic asphyxia. Just before death the pupils dilate as the result of asphyxia. From 3 to 5 grains (0.2–0.3 gm.) of morphin, if retained, is usually a fatal dose, although patients sometimes recover after the ingestion of much larger quantities.

Treatment of Acute Opium-poisoning.—The stomach should be emptied by means of the stomach-pump or a stimulating

emetic, such as zinc sulphate or mustard flour. Since morphin is eliminated by the stomach and then reabsorbed, lavage should be repeated at short intervals. Black coffee may be given by the mouth or by the rectum; it promotes wakefulness and also stimulates respiration. The best chemical antidote is potassium permanganate; 3 to 5 grains (0.2–0.3 gm.) of this drug, dissolved in a glassful of water, should be given at once and repeated in thirty minutes. Tannin is also used as a chemical antidote. The best physiologic antidotes are the powerful respiratory stimulants, such as atropin, strychnin, and caffein; one or all of these may be given hypodermically in full doses.

Artificial respiration is of the greatest value, and should be maintained so long as the beating of the heart continues. It is necessary that the patient should be aroused and kept awake, so that he himself can aid in keeping up respiration. Flicking with a wet towel, the use alternately of hot and cold water, and the application of the faradic current are among the measures that may be employed in staving off sleep. In carrying out the treatment it is important to avoid chilling or exhausting the patient.

Chronic opium-poisoning is usually acquired by taking opium, morphin or heroin for the relief of pain or insomnia or by associating with addicts. Unfortunately, the physician himself is responsible for many cases. Neurotic individuals are especially susceptible, but normal persons not rarely become habituated to the use of opiates by taking them over a considerable period of time. According to Petty, the average person acquires an addiction to morphin when the drug is used daily for a month. Morphin may be used for a longer time without causing the habit when taken by the mouth than when taken hypodermically, the difference in this respect depending upon the rate of absorption and hence upon the strength of the narcotic impression. Codein very rarely leads to habituation in the ordinary sense of the term. Habituated are able to withstand enormous doses of an opiate without suffering from acute poisoning, this tolerance being due partly to an increase in the power of the organism to destroy the drug and partly to an increase in the power of resistance. The average daily oral dose of morphin for an addict is probably between 5 and 15 grains, but the daily consumption may be as high as 90 grains (McIver and Price). A large proportion of addicts begin the use of drugs while still minors. Opium itself may be taken by the mouth or inhaled as smoke; morphin may be introduced by the mouth or by hypodermic injection; heroin is usually sniffed up the nostrils.

If he is careful as to dosage, the addict may get along fairly well for years, without even his family or his associates being aware of

his habit. In 3 of the cases studied by McIver and Price the duration of the addiction was over 30 years. Sooner or later, however, a more or less characteristic condition is produced, the important features being a cachectic appearance, with a pale, dry skin, disturbed digestion, obstinate constipation, or constipation alternating with diarrhea, loss of flesh and strength, restlessness, irritability of temper, moodiness, with transitory periods of depression and exaltation, impairment of intellect, loss of will power and of ethical sense, and moral perversion, this last being much more pronounced, as a rule, than in alcoholism. In advanced cases the body is emaciated, the skin is sallow or pale and wax-like, the pupils are moderately dilated, the lips, tongue and hands are tremulous, the gait is unsteady, and the whole appearance of the patient is that of premature senility. Neuralgias and paresthesias are almost always present and impotence is common. If the drug is taken hypodermically the site of each needle puncture is shown by a minute bluish-white cicatrix. The systemic effects of heroinism are usually less severe than those of morphinism.

When the habitu   does not get his usual dose he invariably develops a group of distressing symptoms, the most constant of which are restlessness, depression, an intense craving for the drug, yawning, sneezing and lacrimation, and later vomiting, diarrhea, pains in the abdomen and limbs, profuse perspiration, exhaustion and not rarely collapse. These symptoms, which probably depend upon the formation of some unidentified toxic substance, vary in severity with the size of the dose that the patient has been taking and the rapidity with which the drug is withdrawn.

Withdrawal of the narcotic is not excessively difficult and lasting recovery is by no means impossible, but the large majority of patients, even after they have been off of the drug for months, relapse.

Treatment.—Isolation in a special hospital or sanatorium is almost imperative, and the detention should be for at least a year. To avoid deception, the patient must be under the close observation of a reliable attendant throughout the entire course of treatment. As a rule, the opiate should be withdrawn rapidly (in from ten days to two weeks), but in severe cases not too abruptly for fear of collapse. The diet should consist of nutritious and easily digestible food, milk and eggs being most suitable at first. Free and persistent purgation is requisite. Hot baths and the administration of bromids may be employed to control nervousness; salicylates and acetphenetidin, to relieve pains; and scopolamin, trional and codein to produce sleep. Vomiting is

best relieved by gastric lavage and the administration of bismuth subcarbonate. For circulatory weakness digitalis and strychnin are the most useful remedies. Massage, graduated exercise, a liberal diet and tonics are indicated in the convalescent stage.

Several special methods of treatment have found more or less favor, but no one method is applicable to all cases. The Lambert-Towns method consists in a rapid withdrawal of the narcotic and the administration of powerful cathartics (compound cathartic pills, blue mass, and salines) at frequent intervals, in conjunction with a mixture of belladonna, xanthoxylum, and hyoseyamus, which is given every hour, day and night, until signs of belladonna poisoning develop. In the Sceleth method the patient is given a mixture of dionin, scopolamin, pilocarpin and cascara sagrada, the doses varying with the amount of morphin the patient has been taking. On the tenth day this combination is stopped and strychnin nitrate is substituted. In the Petty method large doses of strychnin are given hypodermically in conjunction with scopolamin.*

Therapeutics.—Morphin is used to relieve pain and distress, to induce sleep, to allay cough, to lessen dyspnea, to check excessive peristalsis, to suppress convulsions, to facilitate anesthesia, to promote diaphoresis, to control vomiting and to favor the arrest of hemorrhage.

To Relieve Pain and Distress.—Morphin is the most efficient of all analgesics. In relieving the severe pain of gross lesions—*malignant growths, acute inflammation of serous membranes, fractures, etc.*—it has no rival. In *neuralgia* and other forms of recurrent pain it should be used only after all other measures have failed, and then with extreme caution, since the danger of forming the opium habit in these cases is very great. In the painful crises of *locomotor ataxia* its use may become imperative. Osler regards morphin, hypodermically, as the most useful drug in those attacks of *angina pectoris* in which amyl nitrite proves ineffective.

In various forms of *colic*—renal, biliary, and intestinal—it is advisable to combine atropin with morphin, since the former aids in relaxing the spasm.

Acute inflammation of the brain and its membranes cannot be considered, as was formerly the case, a contraindication to the use of opium; indeed, in *cerebrospinal fever* and other forms of *acute meningitis* it may be the only remedy that will afford relief from the intense suffering. In *acute appendicitis* morphin should, as a rule, be withheld, since it masks the symptoms and thus interferes with an accurate study of the local conditions.

* These various methods of treatment are fully described in the Jour. Amer. Med. Assoc., Mar. 20, 1915.

In *decompensated valvular disease of the heart* it is invaluable in relieving the dyspnea and general discomfort, dispelling apprehension, and promoting restorative sleep. To secure the best results it should be given hypodermically. For nocturnal attacks of dyspnea (cardiac asthma) occurring in chronic *myocardial disease* injections of morphin with atropin are also exceedingly useful.

Opium is frequently employed in the form of suppositories or enemas in *cystitis*, *dysentery* etc., but as the drug subdues pain solely by depressing the cerebrum, it acts more promptly when given subcutaneously or by the mouth. The use of lotions containing laudanum in erysipelas, articular rheumatism, sprains, etc., is irrational. A weak alcoholic lotion would probably act equally well.

To Induce Sleep.—While opium will relieve insomnia from almost any cause, it is especially suitable for sleeplessness due to *pain*. It is often of service, however, in the *acute infectious diseases*, and in many cases of *manic-depressive insanity* it may be used with advantage to tide the patient over critical periods. Occasionally, owing to a peculiar idiosyncrasy, opium causes excitement and wakefulness instead of sleep. In states of *extreme nervous excitement* chloral is usually superior to opium, but not infrequently better results are obtained from a combination of opium with chloral than from either drug singly.

To Allay Cough.—No remedy is so useful as opium or one of its derivatives in allaying the irritative cough of *bronchitis* or *pulmonary tuberculosis*. It should not be employed, however, if the cough is regularly accompanied by copious expectoration. In edema of the lungs, except the acute paroxysmal form (so-called cardiac asthma), it is a dangerous drug. In severe cases of *whooping cough* opium may be of value in affording temporary relief and securing restful nights.

To Lessen Dyspnea.—Subcutaneous injections of morphin and atropin relieve the dyspnea not only of decompensated cardiac disease, but also that of *bronchial asthma*. Owing to the great danger of establishing a habit, however, this treatment should be reserved for very severe attacks and administered only by the physician himself. In the last stages of *pulmonary tuberculosis*, when dyspnea is a distressing symptom, opium in some form may be the only effective remedy.

To Check Excessive Peristalsis.—In *acute inflammatory affections of the bowel*, after all irritating matters have been removed, opium is of service in checking the excessive peristalsis. In *cholera infantum* hypodermic injections of morphin ($\frac{1}{100}$ gr.—0.00065 gm.) are sometimes of benefit. Crile asserts that next

to surgical treatment the administration of opium is the most efficacious treatment of *acute diffuse peritonitis*.

To Suppress Convulsions.—In *infantile eclampsia*, if the paroxysms occur in rapid succession and other measures, such as the warm bath and an enema of chloral and a bromid, fail, a hypodermic injection of morphin, $\frac{1}{100}$ to $\frac{1}{60}$ grain (0.0006–0.001 gm.) for an infant of 1 year, will often yield good results. Mackenzie, Loomis, and Osler speak favorably of the action of morphin in the convulsions and other nervous manifestations of *uremia*, and undoubtedly the drug may be given with benefit in some cases, but it must always be used with caution, especially in cases of chronic glomerulonephritis.

In spinal convulsions, such as occur in *tetanus* and *strychnin-poisoning*, morphin is much inferior to bromids, chloral, and the general anesthetics.

To Facilitate Anesthesia.—Morphin or morphin with atropin or scopolamin is often given a short time before surgical operation to decrease apprehension, to shorten the preliminary stage of the anesthesia, and to reduce the necessary amount of the anesthetic. Its usefulness is somewhat impaired, however, by its tendency to depress the respiration and to interfere with the pupil reactions as danger signals.

To Promote Diaphoresis.—In the beginning of “colds” opium is sometimes useful for its sudorific effect. Dover’s powder is the best preparation, since the ipecac in it seems in some way to aid the action of the opium.

To Control Vomiting.—Although morphin through a stimulant action on the vomiting center tends to cause nausea and vomiting, full doses are antiemetic and are sometimes effective in controlling refractory vomiting resulting from *irritation of the stomach* or *organic disease of the brain*, such as tumor, meningitis, etc.

To Favor the Arrest of Hemorrhage.—Hypodermic injections of morphin are often employed as an adjuvant to other measures to arrest *bleeding from internal organs* (hemoptysis, enterorrhagia, etc.). The efficacy of the drug depends solely upon its power to quiet the patient and to control involuntary movements, such as coughing, peristalsis, etc.

Untoward Effects.—In some persons the use of opium, even in moderate doses, is followed by headache, depression, anorexia, nausea, and vomiting. In others, on account of a peculiar idiosyncrasy, it causes excitement and wakefulness instead of sleep. In rare instances it occasions general pruritus or an erythematous rash.

Contraindications.—Opium should not be used in pulmonary affections associated with embarrassed respiration, such

as edema and pneumonia during the stage of consolidation. For reasons already mentioned it is best to withhold it in appendicitis. When chronic nephritis is present it must be used with the utmost circumspection.

Administration.—If a prompt analgesic effect is desired, one of the salts of morphin should be selected in preference to opium, and should be administered hypodermically. If large doses are required it is well to add a small dose of atropin ($\frac{1}{150}$ gr.—0.0004 gm.) to each injection, in order to counteract the depressing effect of the morphin on the respiration. Pulverized opium, deodorized opium, and the extract are suitable preparations for use in pills. Dover's powder is the best preparation for promoting diaphoresis. The most agreeable liquid preparations are the deodorized tincture and paregoric. Paregoric, on account of its weakness and pleasant taste, is especially suitable for children. The disagreeable after-effects of opium are often prevented by combining with it potassium bromid.

Children are especially sensitive to the drug in all forms, and, in consequence, the dose must be considerably less than the age would apparently justify.

Incompatibles.—Ammonia, alkaline carbonates, preparations containing tannin, or salts of the metals should not be prescribed in solution with morphin. Chlorids, bromids, iodids, and borates, if present in large amount, precipitate morphin from solutions. Even dilute hydrocyanic acid may slowly precipitate from solutions of morphin an insoluble cyanid of the alkaloid.

CODEINA, U. S. P.

Among the alkaloids of opium codein (methyl morphin) ranks next in importance to morphin. It occurs in the form of colorless crystals, of a bitter taste, freely soluble in alcohol, but sparingly soluble in water. The sulphate and phosphate are preferred to the alkaloid itself, on account of their ready solubility in water. The phosphate, being soluble in 2.3 parts of water, is adapted to hypodermic use. Codein resembles morphin in its action, but it is much less powerful as an analgesic and somnifacient. On the other hand, it is less constipating than morphin, less prone to cause nausea and vomiting, and very much less likely to induce a habit; indeed, codein addiction, notwithstanding the frequency with which the drug has been used, has rarely been observed. Codein differs from morphin, too, in being excreted by the kidneys, rather than by the stomach and bowel.

Codein is an excellent remedy for relieving mild degrees of *pain* and allaying *irritative cough*.

DIACETYLMORPHINA, U. S. P.

(Heroin)

Diacetylmorphin, or heroin, appears as a white crystalline powder, of a slightly bitter taste, very sparingly soluble in water, but freely soluble in acidulated solutions.

Heroin is more depressant to the respiratory center than morphin, but it is much less powerful than the latter as an analgesic and somnifacient. It is excreted in the urine and feces, and largely unchanged. It is very prone to induce a habit and tolerance to it is readily established. Large doses are not rarely followed by nausea, headache, dryness of the throat, vertigo, and numbness of the limbs. The symptoms of chronic heroinism are similar to those of chronic morphinism.

Heroin is employed chiefly to allay cough in *bronchitis* and *pulmonary tuberculosis*, although it is not generally so efficacious as codein. It is also of service in *bronchial asthma*. It may be dispensed in pills, in powders, or in water to which a small amount of acid has been added. The hydrochlorid (*Diacetylmorphinæ Hydrochloridum*, U. S. P.) is readily soluble in water and may be given by the mouth or hypodermically. The dose of the alkaloid itself or of the hydrochlorid is from $\frac{1}{20}$ to $\frac{1}{8}$ grain (0.003–0.008 gm.).

ÆTHYLMORPHINÆ HYDROCHLORIDUM, U. S. P.

(Dionin)

Ethylmorphin hydrochlorid, or dionin, is a whitish crystalline powder, freely soluble in water. As an analgesic and somnifacient it stands midway in efficiency between codein and morphin. Applied to the eye in a 2 to 5 per cent. solution or 5 per cent. ointment it causes more or less irritation, hyperemia and edema, followed by persistent analgesia. The vascular reaction has been utilized by ophthalmologists to favor the absorption of inflammatory exudations.

As an internal remedy dionin has been employed for the same purposes and in the same doses as codein, but it has no advantages over the latter. As a local remedy, it has been well recommended as analgesic and absorbent in certain inflammatory diseases of the eye, especially *iritis* and *interstitial keratitis*. Patients should be warned that applications are likely to cause congestion of the conjunctiva and swelling of the eyelids. These effects soon subside and are of no serious import.

PAPAVERINA

Papaverin has an action on the central nervous system similar to but very much milder than that of morphin. Qualitatively, its action differs from that of morphin in relaxing smooth muscle in the stomach, intestines, ureters, bile-ducts, arteries, bronchi, etc., and in producing an analgesic effect when applied to mucous membranes or when injected beneath the skin. In large doses, it also lowers the bloodpressure by relaxing the arterial muscle.

The hydrochlorid of papaverin, which is soluble in water and in alcohol, has been recommended as an antispasmodic in *pylorospasm*, various *colics* (*renal*, *biliary* and *intestinal*), *dysmenorrhoea*, *asthma*, etc., and as vasodilator in *angina pectoris* and *arterial hypertension*. It may be given subcutaneously or by the mouth in doses of $\frac{1}{2}$ to 2 grains (0.03–0.13 gm.). A 2 per cent. solution of papaverin, injected through a ureteral catheter, has been successfully employed to relax the ureter and to release impacted calculi.

PANTOPON

Pantopon is a mixture of the hydrochlorids of the natural alkaloids of opium in the proportion in which they exist in Smyrna opium. It contains about 50 per cent. of anhydrous morphin hydrochlorid. Being free from gum, resin, etc., it is more rapidly absorbed than opium and may be given hypodermically. One grain (0.065 gm.) is equivalent to 5 grains (0.32 gm.) of powdered opium or to 0.6 grain (0.035 gm.) of morphin sulphate. The dose is from $\frac{1}{8}$ to $\frac{1}{2}$ grain (0.008–0.03 gm.).

CANNABIS, U. S. P.

(Cannabis Indica, Indian Hemp, Hashish*)

The flowering tops of an East Indian plant, *Cannabis sativa*. It contains a resinous principle known as *cannabinol*.

PREPARATIONS	DOSE
Tinctura Cannabis, U. S. P.	10–30 min. (0.6–2.0 mils)
Fluidextractum Cannabis, U. S. P. .	1–5 min. (0.06–0.3 mil)
Extractum Cannabis, U. S. P.	$\frac{1}{8}$ – $\frac{1}{2}$ gr. (0.008–0.03 gm.)

Pharmacologic Action.—Cannabis in large doses produces a condition of mental exhilaration associated with hallucinations and disordered consciousness of time, locality, and personality. This stage of excitement finally gives way to sleep, which may

* Hashish is probably a corruption of the Sanskrit word *Khashkhash*, which means poppy-seed, opium and cannabis indica at an early date having been confused with each other.

last several hours. Sensation is perverted and benumbed, and before sleep is induced there is often more or less general hypesthesia. Upon the circulatory and respiratory systems the drug has little influence unless given in very large doses.

Although alarming symptoms sometimes follow overdoses of cannabis, no death from its use has been recorded.

Therapeutics.—Cannabis is used chiefly as a mild analgesic, sedative, and somnifacient. Although much inferior to opium, it may replace the latter when, for any reason, the use of the more active drug is undesirable. It is sometimes efficient in the persistent cough of *chronic bronchitis* and *pulmonary tuberculosis*, in the dyspnea of *asthma*, and in the restlessness and insomnia of *chronic nephritis*. As an analgesic it is valuable in certain forms of *headache*, especially *migraine*, in which affection it is not only useful between, but also during, the paroxysms. It is occasionally effective in relieving the pains of *locomotor ataxia*. In some forms of *dysmenorrhea* it proves serviceable. In combination with the bromid of potassium it is sometimes useful in *mania* and *delirium tremens*.

Administration.—As the preparations of cannabis vary considerably in strength, and as some individuals are much more susceptible to the action of the drug than others, it is always advisable to begin with small doses and to increase them gradually. A dose of 10 drops of the tincture, repeated in four hours, has caused in an adult intense excitement, dilatation of the pupils, and disordered sensation.

As the addition of water or of an aqueous liquid to the fluid-extract or tincture precipitates the resinous principle, an alcoholic menstruum should be selected for these preparations, or, in case water is used, enough mucilage should be added to hold the resin in suspension.

CHLORALUM HYDRATUM, U. S. P.

(Hydrated Chloral, Chloral, $\text{CCl}_3\text{COH} + \text{H}_2\text{O}$)

Hydrated chloral is obtained from the union of a molecule of water with trichloraldehyd (chloral), the latter being a product of the action of chlorin on alcohol. It occurs in the form of colorless, transparent crystals, having a bitterish, caustic taste, a pungent odor, and a neutral reaction. It is freely soluble in water, alcohol, ether, or chloroform. When triturated with camphor or menthol it liquefies. The dose is from 10 to 30 grains (0.65–2.0 gm.).

Pharmacologic Action.—**Nervous System.**—The dominant action of chloral is on the central nervous system and qualitatively resembles that of chloroform. In moderate doses (15–20

gr.-1.0-1.3 gm.) it depresses the cerebrum without sensibly disturbing the circulation and respiration, and produces a natural sleep lasting from four to eight hours. Unlike morphin, it has but little effect on the algesic centers of the brain, and, therefore, pain antagonizes its soporific action. Larger doses of chloral (30-40 gr.-2.0-2.6 gm.) depress all the cerebral centers, including the motor, and cause profound sleep. Doses of this size also diminish somewhat the reflex excitability of the spinal cord and depress the respiratory and vasoconstrictor centers in the medulla. Toxic doses produce all the phenomena observed in chloroform-poisoning. On the peripheral nerves chloral has but a feeble depressant action.

Circulatory System.—Moderate doses of chloral do not affect the circulation, but large doses lower the bloodpressure by depressing the vasoconstrictor center and the cardiac muscle.

Respiratory System.—The respiration is not affected by ordinary doses of chloral, but after large doses it becomes infrequent and shallow, and, finally, ceases from paralysis of the respiratory center.

Temperature.—Toxic doses lower the temperature by dilating the cutaneous vessels (increased dissipation of heat) and by diminishing muscular movements (decreased production of heat).

Metabolism.—The prolonged use of chloral is followed by increased destruction of protein and by fatty degeneration of the viscera.

Local Action.—Locally, chloral is an active irritant, especially to mucous membranes. Unless taken in dilute solution it is likely to cause nausea and vomiting. Rubbed into the skin, it produces redness and a sense of heat, and later a slight benumbing effect.

Action on Lower Organisms.—Chloral has considerable antiseptic power and even small amounts will prevent the putrefaction of urine and other fluids containing organic matter.

Absorption and Elimination.—Chloral is rapidly absorbed from the gastrointestinal tract, and produces its effect as chloral, the alkalinity of the blood not being sufficient to decompose it into chloroform. It is excreted chiefly in the urine as urochloralic acid, which is a combination of chloral with glycuronic acid. In the urine urochloralic acid or other compounds of glycuronic acid may give a reaction with Fehling's solution similar to that of glucose.

Toxicology.—Acute chloral-poisoning is characterized by coma, shallow and infrequent breathing, extreme muscular relaxation, and collapse. It is distinguished from morphin-poisoning by the early collapse and the absence of minutely contracted

pupils. Death is due to respiratory failure, the direct depressant action of the drug on the respiratory center being augmented by the low bloodpressure in the medulla.

Treatment of Acute Poisoning.—The temperature must be maintained by external heat. Brunton and Stricker found that animals could stand very much larger doses of chloral if the body temperature was kept up artificially than when it was allowed to fall. Cardiac and respiratory stimulants, such as caffein, ammonia, camphor, etc., should be used freely. Intravenous injections of warm saline solution may prove useful by favoring excretion. Artificial respiration is helpful and should be employed early, before the occurrence of asphyxia.

Chronic Chloral-poisoning (Chloralism).—The chief symptoms of chronic chloral-poisoning are restlessness and irritability, mental depression, insomnia, various gastrointestinal derangements, impaired nutrition, and certain phenomena resulting from vasomotor paresis, such as erythematous rashes, transitory lividity, ecchymoses, and slight subcutaneous edema.

The *treatment of chronic poisoning* consists in isolation of the patient, the rapid withdrawal of the drug, with temporary substitution of other sedatives, such as bromids and scopolamin, the correction of digestive derangements, the use of general tonics, and the institution of a good hygienic regimen.

Therapeutics.—Chloral is used as a somnifacient and motor depressant.

Somnifacient.—It is a reliable and rapidly acting somnifacient, producing refreshing sleep, usually without any unpleasant after-effects. It is suitable for occasional use in insomnia resulting from overwork, excitement, delirium or fever, provided there is no marked circulatory or respiratory depression. It may often be used with good results in *delirium tremens*, in *mania*, and in the *acute infections*. Even in *lobar pneumonia*, if the circulatory condition is good, it may sometimes be of benefit. In *hypertensive cardiovascular disease*, without pronounced symptoms of myocardial weakness, it often acts better than any other somnifacient. In sleeplessness resulting from pain it is much inferior to morphin. Repeated administration must be avoided, owing to the danger of habituation. The unpleasant taste of the drug is a serious drawback.

Motor Depressant.—In conjunction with bromids, chloral is the best sedative that we possess for the convulsions of *tetanus* and *strychnin-poisoning*. It is sometimes useful also in *infantile eclampsia*, if the paroxysms are repeated at short intervals, and in *uremic* and *puerperal convulsions*. In severe cases of *epilepsy*, in *whooping cough* with frequent and severe paroxysms, and in

chorea insaniens it may often be given advantageously for short periods. It is too depressing, however, for continued use.

Other Uses.—A full dose of chloral is sometimes given to produce relaxation of the uterine cervix, when the first stage of *labor* is unduly prolonged. Chloral-camphor, which is a syrupy liquid prepared by rubbing together equal parts of chloral and camphor may be used locally as an analgesic in *neuralgia*, *myalgia*, and *toothache*. In the form of an ointment containing from 30 to 40 grains (2.0–2.6 gm.) to the ounce (30.0 gm.), it is sometimes efficacious in *circumscribed pruritus*.

Contraindications.—Pronounced circulatory or respiratory weakness, acute nephritis, and acute gastritis are important contraindications. In chronic neuroses the use of chloral is inadvisable, owing to the danger of establishing a habit.

Administration.—The drug is best prescribed in dilute aqueous solution with an agreeable syrup, such as that of orange.

R̄. Chloral hydrati..... ʒi (4.0 gm.)
Tincturæ aurantii dulcis..... fʒiiss (6.0 mils)
Syrupi aurantii..... fʒi (30.0 mils)
Aquæ..... q. s. ad fʒi (60.0 mils).—M.

Sig.—A tablespoonful in water at bedtime. (*Insomnia*.)

R̄. Chloral hydrati..... gr. xvi (1.0 gm.)
Sodii bromidi..... gr. xl (2.5 gm.)
Syrupi aurantii..... fʒvi (22.5 mils)
Aquæ..... q. s. ad fʒi (60.0 mils).—M.

Sig.—A dessertspoonful every four hours. (*For a child of three years with whooping cough*.)

R̄. Morphinæ sulphatis..... gr. iss (0.1 gm.)
Chloral hydrati..... ʒiiss (6.0 gm.)
Syrupi aurantii..... fʒss (15.0 mils)
Aquæ..... q. s. ad fʒi (60.0 mils).—M.

Sig.—A dessertspoonful at bedtime. (*Insomnia with pain*.)

If the stomach is irritable, chloral may be given by the rectum, using a demulcent, such as milk, as the vehicle.

Incompatibles.—Alkalis, alkaline carbonates, and strong solutions of antipyrin. Chloral is rapidly absorbed from concentrated alcoholic solutions and large doses may cause unconsciousness in a few minutes ("knock-out drops").

OTHER CHLORINATED SOMNIFACIENTS

A number of substitutes for hydrated chloral have been introduced with the hope that they might possess all of the advantages of chloral as a somnifacient without any of its disadvantages as a circulatory and respiratory depressant and gastric irritant. In each case, however, what the drug has gained in freedom from

harmful side-actions has been offset by a loss of somnifacient power. The most important of the substitutes are chloralformamid, chlorobutanol, and butyl-chloral hydrate.

CHLORALFORMAMIDUM

(Chloralformamid, Chloralamid, $\text{CCl}_3\text{COH.HCONH}_2$)

Chloralformamid, or chloralamid, is a synthetic compound formed by the union of chloral with formamid (HCO.NH_2). It occurs in the form of colorless crystals, having a bitter taste and soluble in about 19 parts of water or $1\frac{1}{2}$ parts of alcohol. The dose is from 10 to 30 grains (0.65–2.0 gm.).

Pharmacologic Action and Therapeutics.—Chloralformamid is slowly broken up in the body into chloral and formamid, the former producing its usual effects and being excreted in the urine as urochloralic acid. It is believed that the formamid, owing to its stimulant properties, may counteract to some extent the depressant action of the chloral on the heart and medullary centers. The drug is less irritant to the stomach than chloral, but also less powerful, less prompt, and less certain in its action as a somnifacient. It has no cumulative effect, and patients do not readily become addicted to its use. It is often of service in the milder forms of insomnia occurring at times in *chronic diseases of the heart, lungs or kidneys*, in *acute infections*, and in *senility*. It has been recommended also in seasickness.

Administration.—Chloralformamid may be prescribed in cachets, capsules, or powders, or in some aromatic vehicle, to which alcohol has been added to facilitate solution. It is decomposed into its components by hot water. It should be given about an hour before bedtime.

R_x. Chloralformamidi..... ʒiiss (6.0 gm.)
 Elixiris aromatici..... f ʒi (30.0 mls)
 Aquæ..... q. s. ad f ʒii (60.0 mls).—M.
 Sig.—A tablespoonful in water an hour before bedtime.

CHLORBUTANOL

(Chloretone, Chloroform-acetone, $\text{CCl}_3\text{C}(\text{CH}_3)_2\text{OH}$)

Chlorbutanol is a compound formed by the addition of a caustic alkali to equal weights of chloroform and acetone. It is a white crystalline powder, with a camphoraceous odor and taste. It is sparingly soluble in water, but freely so in alcohol or ether. The dose is from 5 to 20 grains (0.3–1.3 gm.).

Pharmacologic Action and Therapeutics.—Chlorbutanol is a somnifacient and, when applied to mucous membranes and raw surfaces, a mild analgesic and anesthetic. As a somnifacient,

it acts promptly, usually within an hour after its administration, and beyond causing slight drowsiness on the following day, rarely gives rise to any unpleasant after-effects. It is probably more depressant to the circulation and respiration than chloral, but unlike the latter it is a gastric sedative rather than an irritant. Tolerance is somewhat rapidly acquired by repeated administration. The drug may be used in mild forms of *insomnia* unattended with severe pain, high fever, or pronounced mental excitement. It has been employed with some success as a sedative in *seasickness* and *nocturnal epilepsy*. It may be prescribed in cachets, capsules or powders. Locally, it has been recommended in solution or powder as an analgesic and antiseptic application for *burns* and *painful ulcers*. It is sometimes used also as a preservative of solutions of organic drugs, such as epinephrin, homatropin, etc. In the laboratory it is sometimes used as a general anesthetic for small animals, a concentrated alcoholic solution being administered through a stomach-tube.

BUTYL-CHLORAL HYDRAS

(Butyl-chloral Hydrate, Croton-chloral Hydrate, $\text{CH}_3\text{CHC.CC}_2\text{CH (OH)}_2$)

Butyl-chloral is an oily liquid formed by the action of chlorin on acetic aldehyd. It is converted into the solid butyl-chloral hydrate by the addition of water. Butyl-chloral hydrate occurs in the form of white pearly scales having a pungent odor and an acrid, disagreeable taste. It is sparingly soluble in water, but freely so in glycerin or alcohol. The dose is from 5 to 20 grains (0.3–1.3 gm.). It is best given in capsules or cachets, or dissolved in aromatic elixir.

The drug has an action similar to that of hydrated chloral, but it is more irritant to the stomach. Because Liebreich, who introduced it, taught that it had a selective analgesic action on the fifth nerve it has been somewhat extensively employed in the treatment of *trifacial neuralgia* and *migraine*. Liebreich's teaching, however, has been proved to be erroneous.

PARALDEHYDUM, U. S. P.

(Paraldehyd, $(\text{CH}_3\text{COH})_3$)

Paraldehyd is a polymer of acetaldehyd. It is a colorless volatile liquid of a strong ethereal odor and a disagreeable pungent taste. It is soluble in 8 parts of water, and is miscible in all proportions with alcohol, ether, chloroform or oils. The dose is from $\frac{1}{2}$ to 1 fluidram (2.0–4.0 mls).

Pharmacologic Action.—The action of paraldehyd resembles that of chloral, but it is less powerful. The drug is rapidly

absorbed and usually produces a natural sleep without serious depression of the respiration or circulation and without after-effects. It has no analgesic power. In large doses it is prone to disturb the stomach. It is eliminated unchanged through the lungs and kidneys. Toxic doses produce coma, shallow breathing, great muscular relaxation, abolition of reflexes, and finally, death from paralysis of the respiratory center.

Therapeutics.—Paraldehyd is a safe and reliable somnifacient. The chief drawbacks to its use are its unpleasant taste and the disagreeable odor which it imparts to the breath for twenty-four hours after its ingestion. Toleration is somewhat rapidly acquired. It may be employed with advantage in the *insomnia of mania, delirium tremens*, and *hysteria*. It is sometimes efficient as an antispasmodic in *asthma*.

Administration.—It may be administered in cracked ice or in some aromatic vehicle. A few drops of alcohol render it freely miscible with water. The dose should be well diluted.

℞. Paraldehydi,
Glycerini,
Spiritus aurantii compositi..... āā f ʒiv (15.0 mls)
Aquæ..... q. s. ad f ʒij (60.0 mls).—M.
Sig.—A tablespoonful in water, repeated in 3 hours if necessary.

SULPHONMETHANUM, U. S. P.

(Sulphonmethane, Sulphonal, $(\text{CH}_3)_2\text{C}(\text{SO}_2\text{C}_2\text{H}_5)_2$)

Sulphonal and trional are methane derivatives containing ethyl-sulphonic— $\text{SO}_2(\text{C}_2\text{H}_5)$ —radicals. Sulphonal contains two ethyl groups and trional contains three. Generally speaking, somnifacients, and anesthetics containing ethyl groups (sulphonal, ether) are less depressing to the circulation and respiration than those containing halogens (chloral and chloroform).

Sulphonal is made by oxidizing a mixture of ethyl hydro-sulphid and acetone. It occurs as a colorless, crystalline powder, free from odor and taste. It is soluble in 365 parts of cold water, 16 parts of boiling water, or 60 parts of alcohol. The dose is from 15 to 30 grains (1.0–2.0 gm.).

Pharmacologic Action.—In moderate doses sulphonal is a pure somnifacient, affecting only the cerebrum. Owing to its slight solubility, it is very slowly absorbed, and when given in the form of a powder its soporific effect may not be manifest for several hours, or, if administered late in the evening, not until the following day. In ordinary amounts it has no effect on the heart or respiration, and only rarely disturbs the stomach. It has no analgesic properties. Drowsiness, headache, vertigo, mental confusion and cutaneous rashes are sometimes observed

after its use. When taken in single doses or in courses not exceeding a week sulphonal may be regarded as a safe somnifacient, rarely producing any unpleasant symptoms. Its prolonged use, however, is not only likely to result in poisoning, but may cause a habit.

Toxicology.—Acute sulphonal-poisoning does not commonly prove fatal, probably because much of the drug escapes from the digestive tract before absorption takes place. Neisser reports the case of a person who took a tablespoonful of the drug, and slept in consequence four days and nights, and then rapidly convalesced; and another patient, aged fifteen years, who took nearly 3 ounces and was unconscious for five days, recovering entirely in eight days. Death, however, has followed the ingestion of comparatively small amounts. Murrell has cited two instances of death from 30 and 40 grains respectively.

The symptoms of *acute poisoning* are headache, vertigo, tinnitus aurium, marked cyanosis, vomiting, diarrhea, shallow breathing, feeble pulse, dilated pupils, unconsciousness, and collapse. The treatment consists in administering saline cathartics and quickly acting stimulants, and in maintaining the body-temperature.

Chronic sulphonal-poisoning has frequently followed the continuous use of the drug for weeks or months. Seventeen out of 20 cases collected by H. C. Wood, Jr., terminated fatally. Probably from the gradual accumulation of the drug in the body, the symptoms often appear abruptly, sometimes even after the habit has been suspended for several days. The chief phenomena of chronic poisoning are a peculiar red coloration of the urine, languor, ataxia, progressive weakness, paralysis, paresthesia, nausea, vomiting, colicky pains, serous diarrhea or obstinate constipation, insomnia, and mental confusion. In unfavorable cases the urine becomes scanty and albuminous, and the exhaustion deepens into collapse. In a fatal case reported by Taylor and Sailer well-marked degenerative changes were found in the liver, kidneys, and heart. The discoloration of the urine, which is of considerable diagnostic import, is due to the presence of hematorphyrin, a compound derived from hematin.

The treatment of chronic poisoning consists in withdrawing the drug at once, and freely administering saline cathartics with alkalis, especially sodium bicarbonate. Hypodermoclysis and enteroclysis with saline solution are also recommended by Wood.

Therapeutics.—Sulphonal is a useful somnifacient in insomnia due to *nervous excitement, mental disease, and acute infections.*

In sleeplessness caused by pain it is ineffective. In chronic diseases of the heart or kidneys, sulphonal, as a rule, should be avoided.

Administration.—Sulphonal is best administered in hot liquid (hot milk, bouillon or tea) and, as its action is slow, it is well to give it two or three hours before sleep is desired. Compressed tablets should be avoided. On account of its tendency to accumulate in the body, it should not be given continuously for more than a week. Even after its administration for several successive days, it is advisable to order a saline cathartic for the purpose of removing from the bowel any portion of the drug remaining unabsorbed.

SULPHONETHYLMETHANUM, U. S. P.

(Sulphonethylmethane, Trional, $\text{CH}_3\text{C}_2\text{H}_5\text{C}(\text{SO}_2\text{C}_2\text{H}_5)_2$)

Trional differs chemically from sulphonal in having three methyl groups, instead of two, replaced by ethyl. It occurs in the form of colorless, crystalline scales, free from odor, and of a bitter taste. It is soluble in 200 parts of cool water, and readily soluble in boiling water, alcohol, or ether. The dose is from 15 to 30 grains (1.0–2.0 gm.).

Pharmacologic Action and Therapeutics.—The action of trional is similar to that of sulphonal. Owing to its greater solubility, however, it is more prompt in its effect, and has less tendency to accumulate in the body. If not used too continuously, it is a safe and reliable somnifacient, suitable for the same class of cases in which sulphonal is most effective. It is best given in some warm vehicle—milk, tea, or whisky—an hour or two before retiring. Occasionally it gives rise to headache, drowsiness, and nausea on the day following its administration. If used continuously for several weeks, it may cause the following toxic symptoms: headache, vertigo, impairment of memory, disordered speech, tremors, nausea, constipation or diarrhea, colicky pains, hematoporphyrinuria, oliguria, and even strangury. These symptoms, however, do not, as a rule, develop so abruptly as they do after the prolonged use of sulphonal. The treatment does not differ from that of sulphonal-poisoning.

ÆTHYLIS CARBAMAS, U. S. P.

(Ethyl Carbamate, Urethane, $\text{NH}_2\text{COOC}_2\text{H}_5$)

Ethyl carbamate, or urethane, was the first of the urea derivatives or esters of carbamic acid to be used as a somnifacient. In addition to urethane, the group now includes barbital (veronal) phenobarbital (luminal), bromural, and a number of other closely related compounds. Urethane is made by the interaction of ethyl alcohol and nitrate of urea. It occurs as colorless tabular crystals, odorless and of cooling saline taste. It is

readily soluble in water, alcohol, ether, or chloroform. The dose is from 15 to 45 grains (1.0–3.0 gm.).

Pharmacologic Action and Therapeutics.—Urethane is a comparatively safe somnifacient, without influence in ordinary doses on the respiration or circulation, but weak and uncertain in action. It has no analgesic effect. Toxic doses are followed by coma, a fall of temperature, weakness of the pulse, abolition of the reflexes, and death from respiratory paralysis. The drug is excreted as urea. It is only of service in *mild forms of insomnia* and has been supplanted by barbitol (veronal). Dana and Jacobi have spoken favorably of its action as an anticonvulsant in some cases of *epilepsy*.

Urethane is incompatible with acids and alkalis. Rubbed with chlorbutanol (chloretone) it liquefies.

Hedonal, which chemically belongs to the same class as urethane, being methyl-propyl-carbinol-urethane, is a crystalline body of a menthol-like taste, almost insoluble in water, but soluble in alcohol or ether. It is an agreeable and safe somnifacient, only suitable, however for very *mild forms of insomnia*, *unaccompanied by pain or excitement*. It is most effective in doses of from 20 to 30 grains (1.3–2.0 gm.).

BARBITAL

(Diethylbarbituric Acid, Veronal, Diethyl Malonyl Urea, $\text{CO}(\text{NH}-\text{CO}_2)-\text{C}(\text{C}_2\text{H}_5)_2$)

Barbital (veronal), like urethane and hedonal, is also a urea derivative. It is a white crystalline powder, odorless, of faintly bitter taste, freely soluble in alcohol, but sparingly soluble in cold water. The dose is from 5 to 10 grains (0.3–0.6 gm.) in hot milk, bouillon or tea, or in capsules followed by hot liquid.

Pharmacologic Action and Therapeutics.—The action of barbital resembles that of sulphonal and trional, but it is more rapid. An average dose, 8 grains (0.5 gm.), usually produces a natural sleep, which begins within an hour and lasts several hours, and which is unaccompanied by any depression of the circulation or respiration. Even comparatively small doses, however, have been followed by collapse. As after-effects, drowsiness, headache, mental confusion, vertigo and nausea are not rarely observed. The drug is excreted chiefly by the kidneys, appearing in the urine partly as urea and partly as unchanged barbital. Excretion is slow and, therefore, cumulative effects, similar to those of trional and sulphonal, may result from prolonged use.

Acute barbital-poisoning is characterized by coma, shallow respiration, evidences of renal irritation, erythematous eruptions,

and collapse; and chronic poisoning by anemia, gastrointestinal disturbances, mental confusion, ataxia, and hematoporphyrinuria. Barbitol may be used with advantage for relatively short periods in many cases of *simple insomnia, unaccompanied by severe pain or pronounced mental excitement*.

The sodium salt of barbitol (sodium diethylbarbiturate), which is also known as *veronal-sodium* or *medinal*, is readily soluble in water, and, therefore, acts somewhat more promptly than barbitol. It may be used in the same doses as barbitol and may be given by the mouth or by the rectum, or even subcutaneously.

PHENOBARBITAL

(Phenyl-ethyl-barbituric Acid, Luminal, $\text{CO}(\text{NH}-\text{CO})_2\text{C}(\text{C}_2\text{H}_5).(\text{C}_6\text{H}_5)$)

Phenobarbital, or luminal, differs from barbitol or veronal in having one ethyl group (C_2H_5) replaced by one phenyl group (C_6H_5). It is a white powder, of slightly bitter taste, and insoluble in water. The dose is from $\frac{1}{2}$ to 5 grains (0.03–0.3 gm.) in capsules or powders.

Phenobarbital has an action similar to that of barbitol. It allays nervousness and produces sleep, but does not relieve pain. It has been used with some success as a somnifacient in *simple insomnia*, but its chief claim for consideration is as a motor depressant in *epilepsy*, in which disease it is often superior to the bromids. The dose required in epilepsy is small, from 1 to 2 grains (0.06–0.13 gm.) at bedtime usually being sufficient. Occasionally, however, it may be necessary to give from $\frac{1}{2}$ to $\frac{3}{4}$ grain (0.03–0.04 gm.) three times a day, although when administered in this way, it not rarely produces a sense of lassitude, dull headache, and even slight vertigo. To avoid accumulation, it is advisable to suspend the treatment for at least a day once a week.

The sodium salt of phenobarbital (*Phenobarbital-sodium*), because of its solubility and more ready absorption, is superior to phenobarbital, but must be given in slightly larger doses. It may also be used hypodermically in doses of 2 to 5 grains (0.13–0.3 gm.).

BROMURAL

(2-monabrom-isovaleryl-urea, $(\text{CH}_3.\text{CH}(\text{CH}_3)\text{CHBrCO})\text{HN}.\text{CO}.\text{NH}_2$)

Bromural occurs in the form of white, tasteless needles, which are readily soluble in hot water, alcohol or ether, but less readily in cold water. The dose is from 5 to 15 grains (0.3–1.0 gm.) in the form of tablets or capsules.

The drug is a mild, but somewhat quickly acting somnifacient, producing a natural sleep of several hours' duration, without appreciable disturbance of the circulation or respiration. It is useful as a nerve sedative and somnifacient in the various *neuroses* and in *mild forms of insomnia*.

Adalin (Brom-diethyl-acetyl carbamide, carbromal) is closely related to bromural and may be used in the same doses and for the same purposes. Owing to its mild action it is especially suitable for children.

POTASSII BROMIDUM, U. S. P.

(Potassium Bromid, KBr)

Potassium bromid occurs as colorless or white cubical crystals, odorless and of a pungent saline taste. It is soluble in 1.5 parts of water or in 250 parts of alcohol. The dose is from 10 to 60 grains (0.65–4.0 gm.).

Pharmacologic Action.—Nervous System.—The Br ion, irrespective of the base with which it is combined, depresses the entire central nervous system, with the exception of the medulla. Its action is persistent, but relatively feeble. Large doses by depressing the psychic functions cause apathy, lapse of memory, and confusion of thought; by depressing the motor areas, lessen the power of stimuli to excite epileptiform convulsions; and by depressing the spinal cord, diminish reflex excitability. Owing to depression of the reflexes, irritation of the fauces does not result in gagging, sexual power is impaired, and muscular tone throughout the body is lowered. The drug is a comparatively feeble somnifacient. It does not compel sleep, like morphin and chloral, but by eliminating worry, anxiety, etc., or allaying nervous excitement it favors the occurrence of sleep. The action of bromids on the cerebrum is opposed to that of caffein, and on the spinal cord, to that of strychnin.

Circulatory System.—In ordinary doses bromids have no direct effect upon the circulation. They sometimes influence favorably, however, cardiac disturbances resulting from abnormal irritability of the central nervous system. Enormous doses depress the heart and vasoconstrictor center. When introduced directly into the circulation potassium bromid, owing to the presence of the potassium ion, is somewhat more depressing to the heart than iodium or ammonium bromid, but when it is administered by the mouth in therapeutic doses no such difference is observed in its action.

Respiratory System.—Therapeutic doses have no effect on the respiratory center, but very large doses depress it. By lessening reflex irritability bromids tend to allay cough.

Alimentary Canal.—Large doses in concentrated solution may cause nausea and vomiting through salt action. On the other hand, bromid in dilute solution is sometimes useful in controlling vomiting of central origin.

Sexual Functions.—By depressing the cerebrum and the spinal cord, bromids diminish or abolish both the sexual appetite and sexual power.

Absorption and Elimination.—Bromids are rapidly absorbed from the gastrointestinal tract and may appear in the urine a few minutes after their ingestion. The rate of excretion, however, is less rapid than that of absorption, hence there is a marked tendency to accumulation in the tissues. The accumulation is influenced materially by the intake of chlorids, the one salt partially replacing the other in the tissues. The free administration of common salt (sodium chlorid) accelerates the excretion of the bromids, and conversely the administration of bromids increases the elimination of the chlorids. Other halogens have a similar action. Large doses of bromids have some diuretic effect through their salt action. Although the elimination of bromids is effected chiefly by the kidneys small amounts leave the body through other channels.

Bromism.—The repeated administration of a bromid leads sooner or later, according to individual susceptibility, to a condition known as *bromism*. An early manifestation is an eruption of pustular acne on the face, chest and back, similar to that produced by iodids. Occasionally, the eruption is furuncular. The cause of the cutaneous disturbance is not definitely known. It is probably due, however, to a peculiar sensitization of the skin by the bromid and not, as was formerly believed, to the liberation of free bromin by the sebaceous glands. Frequent washing, free water drinking, the use of saline laxatives, and the co-administration of arsenic have a preventive influence in many cases.

Even when it produces no rash, the long-continued use of the bromids usually leads to apathy, mental depression, impairment of memory, somnolence, fetor of breath, gastrointestinal derangements, muscular weakness, sexual impotence, and malnutrition.

Acute Bromid-poisoning.—The chief symptoms resulting from the ingestion of a single toxic dose of a bromid are somnolence or actual stupor, ataxia, extreme muscular relaxation and collapse. Apparently, no fatal case of poisoning in a healthy person has been reported.

Therapeutics.—Bromids are used to suppress convulsions and local spasms, to allay abnormal nervous irritability, to decrease sexual hyperesthesia, to check nervous vomiting, to relieve headache and neuralgia, and to produce sleep.

To Suppress Convulsions and Local Spasms.—The bromids are especially effective in the symptomatic treatment of *epilepsy*. They not only exert a direct sedative influence on the cerebral cortex, but through their action on the afferent paths of the spinal cord they protect the cerebrum from the disturbing influence of peripheral stimuli. While they rarely effect a cure, they usually reduce decidedly the frequency of the paroxysms. The amount required varies with the severity of the case and the susceptibility of the individual and must be determined experimentally in each case. Saturation is indicated by mental hebetude, digestive disturbances, and loss of the palatal reflex. The daily dose usually ranges between 1 and $1\frac{1}{2}$ drams (4.0–6.0 gm.). If larger doses than these are required, it is advisable to try a combination of other drugs with the bromid or to substitute some other remedy. Sometimes moderate doses of the fluidextract of *solanum carolinense*, or small doses of antipyrin, or of thyroid extract will serve to lessen the amount of bromid required. In *nocturnal epilepsy* the administration of chlorbutanol (see p. 103) or of chloral, for a short time, may prove efficacious. If the circulation is weak a combination of a bromid with digitalis or *adonis vernalis*, as recommended by Bechterew, will sometimes be found useful. The reduction to a minimum of the salt in food, decidedly increases the efficacy of the bromid treatment.

In some cases of epilepsy it is necessary to withhold the bromids entirely, as the general disturbance that they produce more than counterbalances the good they accomplish in reducing the number of seizures. Frequently, phenobarbital (luminal) or phenobarbital-sodium proves more satisfactory in suppressing the convulsions than the bromids.

The bromids are of value also in other convulsive disorders besides epilepsy, such as *puerperal eclampsia*, *infantile eclampsia*, *strychnin-poisoning* and *tetanus*. In severe cases of *chorea* with incessant movements bromids are sometimes beneficial, but, as a rule, they are less efficient than chloral or scopolamin. In conditions attended with local spasm—*whooping cough*, *laryngismus stridulus*, and *bronchial asthma*—bromids are not rarely of service.

To Allay Abnormal Irritability.—In abnormal nervous irritability arising from various causes the bromids often prove efficacious. They are invaluable for allaying the *unrest resulting from anxiety, worry, and overwork* and that accompanying *hysteria*. In the varied nervous disturbances that attend the *menopause* they are especially useful. They may also be of service in quieting the nervous excitability of *hyperthyroidism* or *exophthalmic goiter*. In fully developed *delirium tremens* they are of little value, but in the stage of excitement preceding the latter they are very efficacious.

To Decrease Sexual Hyperesthesia.—Bromids are reliable anaphrodisiacs and often render valuable service in *satyriasis* or *nymphomania*, *chordee*, and *spermatorrhœa*.

To Check Nervous Vomiting.—Given for several days before the voyage, in doses of from 20 to 30 grains (1.3–2.0 gm.), three times a day, bromids sometimes prevent *seasickness*. They may also be tried in the *vomiting of pregnancy*. Da Costa found that from 30 to 60 grains (2.0 to 4.0 gm.) of potassium bromid, given an hour before a dose of opium, would prevent the disagreeable after-effects of the latter.

To Relieve Headache and Neuralgia.—A bromid in full doses is often serviceable in attacks of *trifacial neuralgia*, *migraine* and *headache due to mental excitement*. In these affections the drug may be combined with acetphenetidin, a salicylate, or caffein. The bromids are also useful in preventing distressing symptoms of *cinchonism*. To be effective, however, three times as much bromid as quinin must be given.

To Produce Sleep.—As direct somnifacients, the bromids are much less active than chloral, morphin, or trional, but in insomnia due to worry or nervous excitement they frequently produce refreshing sleep.

Administration.—The bromids should be given in solution, well diluted, after meals. In epilepsy it is best to divide the daily dose according to the time at which the seizures are likely to occur. Thus, in nocturnal epilepsy comparatively small doses may be given throughout in the day, and a large dose 30 to 40 grains (2.0–2.5 gm.) at supper-time. When the attacks are very frequent and severe antipyrin may be combined with the bromid for a short time, as in the following formula:

℞. Potassii bromidi..... ʒvi (24.0 gm.)
 Liquoris potassii arsenitis..... fʒj (4.0 mls)
 Antipyrinæ..... ʒj (4.0 gm.)
 Aquæ menthæ piperitæ. . q. s. ad fʒvj (180.0 mls).—M.

Sig.—Tablespoonful in water night and morning.

In insomnia from nervous excitement potassium bromid may be combined with chloral, as in the following formula:

℞. Chlorali hydrati..... gr. xl (2.6 gm.)
 Potassii bromidi..... ʒiiss (6.0 gm.)
 Aquæ et syrupi aurantii āā q. s. ad fʒij (60.0 mls).—M.

Sig.—Tablespoonful in water at bedtime.

Incompatibles.—Bromids are incompatible with acids and acid salts. They also precipitate certain alkaloids—morphin, quinin, and strychnin—from neutral solutions. Ammonium bromid is incompatible with sodium nitrite, owing to the forma-

tion of ammonium nitrite, which by decomposing into water and nitrogen may burst the bottle.

AMMONII BROMIDUM, U. S. P.

(Ammonium Bromid, NH_4Br)

Ammonium bromid occurs in colorless crystals or as a white granular or crystalline powder of a pungent saline taste. On exposure to air it liberates bromin. It dissolves in 1.3 parts of water or 12 parts of alcohol. The dose is from 20 to 60 grains (1.3–4.0 gm.), in solution, well diluted. It has no advantages over the corresponding potassium salt, the action of which it closely resembles.

SODII BROMIDUM, U. S. P.

(Sodium Bromid, NaBr)

Sodium bromid occurs in colorless or white cubical crystals, or as a white granular powder, odorless, and of a saline, bitter taste. It is soluble in 1.1 parts of water or in 16 of alcohol. The dose is from 20 to 60 grains (1.3–4.0 gm.), in solution, well diluted. It has an action similar to that of potassium bromid, but is slightly less irritant to the stomach and has a somewhat less unpleasant taste. It may be substituted with advantage for the potassium salt in all conditions in which a bromid is indicated.

STRONTII BROMIDUM, U. S. P.

(Strontium Bromid, $\text{Sr Br}_2 \cdot 6\text{H}_2\text{O}$)

Strontium bromid occurs in colorless, deliquescent crystals, odorless and of a bitter, saline taste. It is readily soluble in water or in alcohol. The dose is from 20–60 grains (1.3–4.0 gm.). It has an action similar to that of the potassium salt, but is somewhat less irritant to the stomach and less powerful. It may be used as a succedaneum for other bromids when the stomach is irritable or when only a mild effect is required.

LITHII BROMIDUM, U. S. P.

(Lithium Bromid, LiBr)

Lithium bromid is a white, granular, deliquescent salt, having a sharp bitter taste. It is freely soluble in water and in alcohol. The dose is from 20 to 60 grains (1.3–4.0 gm.). It has no advantages over the corresponding sodium and potassium salts, which it closely resembles in action.

ACIDUM HYDROBROMICUM DILUTUM, U. S. P.

(Diluted Hydrobromic Acid, HBr)

Diluted hydrobromic acid is an odorless, colorless liquid, of acid properties, composed of 10 per cent. by weight of absolute hydrobromic acid and 90 per cent. of water. The dose is from 15 to 60 minims (1.0–4.0 mils), well diluted. It has an action similar to that of the alkaline bromids, but it is less powerful and much more irritant to the stomach.

BROMOFORMUM, U. S. P.

(Bromoform, Tribrommethane, CHBr_3)

Bromoform is a heavy liquid resembling chloroform, made by the action of sodium hypobromite on acetone or of bromin on a mixture of methyl alcohol and milk of lime. It is a colorless liquid having an ethereal odor and a sweetish taste. It is sparingly soluble in water, but freely miscible with alcohol or glycerin. The dose is from 1 to 5 minims (0.06–0.3 mil).

Therapeutics.—Bromoform has anesthetic properties similar to those of chloroform, but as a therapeutic agent it has been used chiefly as an internal remedy in *whooping cough*. While it is of some value in lessening the severity of the paroxysms, it has no power to shorten the duration of the disease.

Toxicology.—Many cases of poisoning by bromoform have been reported since its first introduction as a remedy for whooping cough. Very often the accident has resulted from a lack of familiarity with the physical properties of the drug. As bromoform is heavier than mucilage, its suspension in the latter can only be temporary; it naturally tends to fall to the bottom of the bottle, and unless this is prevented by frequent and thorough shaking, a much larger dose may be taken on emptying the bottle than was intended. The chief phenomena are coma, cyanosis, marked dyspnea, muscular relaxation and collapse. *Treatment* consists in the evacuation of the stomach, and the administration of cardiac and respiratory stimulants.

Administration.—Bromoform may be administered by simply dropping it on sugar or into a little peppermint-water. On account of its high specific gravity a minim is equal to about 6 drops. If suspended in mucilaginous liquids, the bottle must be well shaken before each administration. As it is soluble in alcohol and glycerin, a mixture of these liquids may be made the vehicle for it.

OTHER BROMIN DERIVATIVES

Bromipin.—This is an addition product of sesame oil containing about 10 per cent. of bromin. The dose is from 1 to 2 drams

(4.0–8.0 mils) in an agreeable emulsion. It acts like the alkaline bromids, but is somewhat less irritant to the stomach, and, as the bromin is split off from it slowly in the intestine, its action is less powerful and more slowly produced.

Bromural.—This is a compound produced by the interaction of urea with brom-isovaleryl bromid. The dose is from 5 to 15 grains (0.3–1.0 gm.). It is a mild somnifacient and nerve-sedative (see p. 109). *Adalin* (see p. 110) is a closely related compound.

Brometone (Tribrom-tertiary-butyl alcohol) is the product of the reaction of acetone with bromoform. It is a white, crystalline substance, with a camphoraceous odor and taste, and soluble in alcohol, but only slightly so in water. It acts like the inorganic bromids, but is said to be less irritant to the stomach and less likely to produce bromism. The dose is 5 grains (0.3 gm.) in powder or capsule.

Bromids of the heavy metals, such as bromid of gold, and *bromids of the alkaloids*, such as bromid of quinin, have no bromin action.

SCOPOLAMINÆ HYDROBROMIDUM, U. S. P.

(Hyoscin Hydrobromid)

Scopolamin (see p. 80) is a useful somnifacient when sleeplessness is accompanied by marked mental or motor excitation. Thus, it often yields satisfactorily results in *delirium tremens*, *chorea insaniens*, *melancholia agitata* and *mania*. The dose is from $\frac{1}{200}$ to $\frac{1}{100}$ grain (0.0003–0.00065 gm.).

The optically inactive scopolamin hydrobromid, which has been introduced under the name *euscopol*, has the same effect on the cerebrum as the official or optically active scopolamin hydrobromid, but its peripheral actions (depression of the oculomotor, vagal and secretory nerve-endings) are much weaker.

GENERAL ANESTHETICS

General anesthetics are drugs which acting on the nervous system in concentrated form rapidly produce unconsciousness and insensibility. They are employed to abolish or lessen pain and to relax spasm. They are used for both of these purposes in surgical operations, in labor, and in severe attacks of colic (renal, biliary, etc.). They are of service in subduing the violent convulsive seizures of tetanus and strychnin-poisoning. By suspending muscular irritability they also render valuable aid in the reduction of luxations, fractures, and strangulated hernias, and in the recognition of deep-seated abdominal lesions. General anesthesia is hazardous in the presence of profound

shock, serious uncompensated disease of the heart, the *status lymphaticus*, acute nephritis and large tumors interfering with the respiration and circulation. The most important general anesthetics are:

Ether
Chloroform

Nitrous oxid
Ethyl chlorid.

History.—Ether was first used as an anesthetic in surgical procedure by C. W. Long, of Georgia, a graduate of the University of Pennsylvania, in 1842. The first public demonstration of ether narcosis in surgery, however, was made by William Morton and John Collins Warren, in the Massachusetts General Hospital, in 1846. Since the latter date it has been, in this country, the most extensively used general anesthetic in all operations, excepting the most trivial.

Sir James Y. Simpson, of Edinburgh, employed chloroform for the first time as a general anesthetic in 1847. Sir Humphry Davy, of Penzance, England, suggested the use of nitrous oxid as an anesthetic for surgical operations in 1800, but the first actual tests of the gas were in dentistry in 1844 by Horace Wells, of Hartford, Connecticut. The term "Anesthesia" seems to have been first proposed by Oliver Wendell Holmes.

ÆTHER, U. S. P.

(Ether, Ethyl Oxid, (C₂H₅)₂O)

Ether is produced by distilling a mixture of sulphuric acid and alcohol, and appears as a colorless, volatile, highly inflammable liquid, having a characteristic odor and a burning sweetish taste. It is soluble in about 12 parts of water, and is readily miscible with alcohol, chloroform or oils. The official preparation contains about 4 per cent. of alcohol.

PREPARATIONS

DOSE

Spiritus Ætheris, U. S. P. (32.5 per cent.).....	½-1 fl. dr. (2.0-4.0 mls)
Spiritus Ætheris Compositus (Hoffmann's anodyne: Ether, 32.5 per cent. and Ethereal Oil, 2.5 per cent.).....	½-1 fl. dr. (2.0-4.0 mls)

Pharmacologic Action.—When freely inhaled ether first causes smarting in the nose and throat, coughing, a sensation of suffocation and increased secretion of mucus and saliva. These symptoms are soon followed by flushing of the face, injection of the conjunctivæ, dilatation of the pupils, irregularity in breathing, impairment of sensibility (*partial analgesia*), and an increase in the rate and strength of the pulse. Frequently, emotional excitement develops, characterized by shouting, crying, laugh-

ing, or violent struggling. Retching or actual vomiting may also occur. Later, if the administration of the ether is continued in sufficient concentration, complete unconsciousness ensues, with muscular relaxation, moderate contraction of the pupils, regular and usually snoring or stertorous breathing, slight cyanosis, abolition of most of the reflexes, some lowering of the body-temperature and sweating. The pulse during this stage (*anesthetic stage*) is full and somewhat frequent, and, unless the anesthesia is of long duration, the blood pressure is well maintained. With still deeper narcosis, symptoms of *collapse* supervene. The face becomes pale or deeply cyanosed, the pupils widely dilate, the pulse becomes weak and irregular, the respiration becomes labored and shallow, a cold clammy sweat appears, the sphincters relax and death occurs, usually from failure of respiration.

Circulatory System.—The increase in the rate and strength of the pulse observed at the beginning of anesthesia is due in part to general excitement and partly to reflex stimulation of the heart from irritation of the air passages. Hypodermic injections of ether, as of alcohol, may also cause transient stimulation of the heart by inducing local irritation. The drug probably never directly stimulates the heart. In ordinary surgical anesthesia the cutaneous vessels are dilated, the pulse-rate is somewhat accelerated, and the blood pressure is well maintained. In the paralytic stage of anesthesia the blood pressure falls, owing to depression of the vasoconstrictor center and heart. The sudden arrest of the heart from reflex or direct vagus stimulation that sometimes occurs in early chloroform anesthesia is not observed with ether.

Respiratory System.—The irregular breathing often noted at the commencement of anesthesia is due partly to excitement and partly to irritation of the air passages. The failure of respiration occurring from overdoses of ether is the result of direct depression of the respiratory center, though in the majority of cases low blood pressure in the medulla is an important contributing factor. Unless the cardiac weakness is too pronounced, respiratory failure can nearly always be overcome by artificial respiration. It should be borne in mind that the ill effects of ether on both the respiration and circulation are much more closely related to the degree of concentration in which it is administered than to the actual amount of it inhaled.

Nervous System.—Ether directly depresses the entire central nervous system, the cerebrum being first affected, then the spinal cord, and last of all the medulla. The sensory neurons are acted upon before the motor. About 20 per cent. (volume) of

ether must be present in the inspired air to establish anesthesia in human beings, and from 6 to 10 per cent. (volume) must be present to maintain the anesthesia. The actions of ether on the nervous system and circulation are qualitatively similar to those of alcohol.

Eye.—During the induction of the anesthesia the pupils are dilated from excitement. In the period of complete anesthesia they are somewhat contracted and the eye reflexes are absent. In the paralytic stage the pupils are widely dilated. Dilatation of the pupils with return of the corneal reflex usually indicates recovery from the anesthesia and calls for a more free administration of ether, but sudden dilatation of the pupils without any return of the eye reflexes signifies dangerous asphyxia.

Temperature.—Etherization always lowers the body-temperature and, therefore, it is important that the operating room should be well heated and the patient should be guarded against exposure not only during the operation but for several hours afterward. The fall of temperature is due partly to increased loss of heat from dilatation of the cutaneous vessels, and partly to decreased production of heat from absence of muscular movements.

Blood.—Ordinary anesthesia often causes a slight and transitory polycythemia, probably by reducing the plasma of the blood. Some diminution of hemoglobin may also occur, as a result of increased hemolysis, if the anesthesia is prolonged.

Alimentary Canal.—In small amounts, well diluted, ether acts as a carminative, promoting the expulsion of gas and relieving colic. Undiluted, it produces a burning sensation in the stomach and sometimes vomiting. Large quantities through rapid volatilization may also cause dangerous distention of the stomach. The nausea and vomiting commonly observed after etherization may be partly a central effect and partly a local effect of ether that has been swallowed with mucus and saliva.

Local Action.—When applied to the skin, ether evaporates quickly, produces intense cold, and thus benumbs the peripheral nerves. Local irritation, sometimes sufficient to cause inflammation and even vesication, may follow if the evaporation is prevented. Inhaled, it causes irritation of the mucous membrane of the respiratory tract, and thus induces a reflex secretion of saliva and mucus. As stated above, the vomiting observed as a sequel of etherization may be due in part to irritation of the stomach by ether that has been swallowed with the saliva.

Absorption and Elimination.—Ether is absorbed rapidly from the lungs and also from the stomach and rectum. It is excreted promptly and for the most part by the lungs, although a small

amount is excreted by the kidneys. On the latter the drug has an irritant effect, and, therefore, considerable caution must be exercised in its employment as a general anesthetic when there are evidences of serious nephritis. After prolonged anesthesia the urine may contain not only albumin and casts, but also certain bodies the result of disturbed metabolism, such as glucose and acetone.

ADMINISTRATION OF ETHER AS AN ANESTHETIC.—In using ether as a general anesthetic the following precautions should be observed: no solid food should be allowed for 12 hours, nor liquid food for 4 hours, before the operation. Unless the bowels have been freely moved within 24 hours an enema should be given a few hours before anesthesia is induced. When an anesthetic is given to a female a third person should always be present. Before administering the ether the teeth should be examined, and, if artificial, they should be removed. To guard against aspiration pneumonia it is advisable also to cleanse the mouth thoroughly with an antiseptic wash before operation. The throat and waist should be free from tight clothing, but the patient should not be exposed to a loss of heat, as pneumonia is likely to follow if this precaution is unheeded.

The anesthetizer must guard against placing the head and arms of the patient in positions likely to cause pressure on nerve-trunks. The eyes should be covered with a pad of moistened gauze and the lips and nostrils anointed with petrolatum to protect them from the irritant action of the ether. As the vapor of ether is highly inflammable, and since it is heavier than air, it is necessary when operating by gas-light to have the jet above the operator. No more ether should be used than is absolutely necessary to induce and maintain the desired degree of anesthesia. The anesthetizer should be continually on the lookout for any irregularities in the respiration or pulse and for changes in the eye and facial color.

Ether may be administered from a towel loosely folded in the form of a cone, surrounded by stiff paper, and enclosing at its tip a small sponge, or, better, from an open inhaler made especially for the purpose. The inhaler of Allis is simple and economical. At first the inhaler should be held some distance from the nose, to accustom the patient to the irritant effects of the ether, but soon it should be brought close to the nose, so that the anesthetic may be inhaled in a more concentrated form. Regular snoring respiration, muscular relaxation, and insensibility of the conjunctiva are the indications that the patient is prepared for the operation. Administration by the "open drop method," which is now adopted in many hospitals, has much

to recommend it. It consists in pouring ether, drop by drop, at the rate of about 150 drops per minute, upon several layers of gauze, supported by a simple wire mask. Complete narcosis is produced in from 8 to 10 minutes. With this method there is much less tendency to coughing, struggling, and retching, the secretion of mucus is not nearly so profuse, and the frequency of after-sickness is notably reduced. The method of administering ether from a closed inhaler that does not permit of a free access of air (closed method) is less safe and less pleasant.

The quantity of ether required for an ordinary operation, lasting about an hour, is usually from 6 to 10 ounces (180–300 mls), more being necessary with the open method than the older one.

Other Methods of Administration.—Intrapharyngeal anesthesia has a definite advantage in operations about the mouth. With this method anesthesia is established in the ordinary way, and then the mask is removed, and the ether administered through a catheter introduced into the pharynx through the nose or mouth. To drive the ether vapor into the lungs a foot bellows or an electric air-pump may be employed. Intratracheal insufflation is carried out in the same way, but the catheter is passed through the glottis into the trachea almost to the bifurcation. It is less simple than the intrapharyngeal method and more dangerous.

The administration of ether by the rectum, using oxygen or olive oil as a diluent, has some advocates. With this method irritation of the respiratory tract and the unpleasant symptoms of the first stage are avoided. Untoward effects, however, sometimes occur, the most common being extreme distention of the bowel and severe colitis. Intravenous administration is entirely feasible, but it is a dangerous method and has few advantages.

Aids to Anesthesia and Anesthetic Sequences.—Morphin, $\frac{1}{6}$ to $\frac{1}{4}$ grain (0.01–0.016 gm.), half an hour before the anesthetic, allays fear, lessens excitement, shortens the first stage of anesthesia, and reduces the amount of the anesthetic required. It should not be used indiscriminately, however, as it increases the danger of respiratory failure, and may interfere with the pupil reactions. It is often of service when the patient is nervous and timid or is addicted to alcohol. It is contraindicated in operations on any part of the respiratory tract, in pulmonary disease, and in all conditions accompanied by pronounced systemic weakness.

Atropin, $\frac{1}{100}$ grain (0.0006 gm.), is sometimes employed to diminish salivation and bronchorrhea and to lessen the danger

of respiratory failure. Its use, however, may interfere with the pupil reactions. Scopolamin, $\frac{1}{120}$ to $\frac{1}{100}$ grain (0.0005–0.0006 gm.), is sometimes given with morphin to intensify its narcotic effects, but it masks the danger signals and adds to the risks.

To avoid the unpleasant features of the first stage of etherization, anesthesia may be induced by some other agent, the action of which is more prompt and agreeable than that of ether, the latter, however, being substituted as soon as the patient has become unconscious. For the preliminary anesthetization chloroform or ethyl chlorid may be selected, but by far the safest agent for the purpose is the combination of nitrous oxid and oxygen.

Accidents during Anesthesia.—The most common accident during etherization is failure of respiration. When this occurs after the first few inhalations, it is generally the result of a reflex *spasm of the laryngeal muscles* excited by the ether. The admixture of a little more air with the vapor will serve to relax the spasm, when respiration will be resumed. Embarrassed respiration is often due to the *accumulation of mucus in the upper air passages or to the tongue falling back into the throat*. In the event of the former accident the head should be turned to one side, when much of the fluid will run out or will collect in the dependent cheek, from which it may be removed by means of a sponge held by forceps. In the event of the latter accident, it will be necessary to press the lower jaw forward and to draw the tongue outward with forceps or the fingers. Finally, respiratory failure may result from the *direct action of the anesthetic on the respiratory center*. Should such an accident occur, the method of treatment to pursue is as follows: Withdraw the ether; lower the head and elevate the legs; push the jaw forward and draw the tongue outward; and practice artificial respiration, persisting in it, if necessary, for at least an hour. If the pulse is also weak, atropin or strychnin should be given hypodermically, but not alcohol, as its action closely resembles that of ether.

Sudden heart failure is a much less common accident under ether than asphyxia. It calls for lowering of the head, hypodermic injections of strychnin, caffein, and atropin, rhythmic compression of the precordium, and artificial respiration. The last serves to remove the ether from the chest, favors the entrance of fresh air, and stimulates the circulation.

After-effects.—The most common after-effect is *nausea and vomiting*. It may be minimized by sequence anesthesia, the preliminary injection of morphin and atropin, and the open drop method of administration. The administration of cracked ice

with a little brandy or of cerium oxalate with sodium bicarbonate will sometimes serve to allay it. In persistent vomiting gastric lavage is often effective. Vomiting that persists despite these measures and is accompanied by signs of collapse is suggestive of acute gastrectasis.

Backache is also common. It may be relieved by the application of hot-water bags and, in the absence of any contraindication, by the administration of a moderate dose of acetphenetidin.

Pneumonia is an occasional sequel. It has been ascribed to exposure of the patient, to chilling of the lungs by the rapid evaporation of the anesthetic, to the irritant action of the ether, to the aspiration of infective secretions from the nasopharynx and, finally, to the lowered vitality of the tissues induced by prolonged etherization. In many cases it is not the result of etherization but of the lodgment of emboli from the field of operation in the vessels of the lung.

Postoperative paresis of the stomach or intestine may occur, but in its production the anesthetic is only a contributory factor. It usually yields to lavage, intestinal irrigation, and the hypodermic injection of pituitary extract or physostigmin.

Paralysis of the Limbs.—Central paralysis from hemorrhage or embolism is rare. Peripheral palsies are not very infrequent, and are due to compression of nerve-trunks. The anesthetic contributes only indirectly to the latter by rendering the patient oblivious to pain.

Contraindications.—The contraindications to the employment of ether as an anesthetic are advanced arteriosclerosis, acute inflammatory infections of the respiratory tract and severe nephritis, especially when associated with cardiovascular lesions. The presence of valvular disease is not in itself a contraindication, provided compensation is well maintained.

Other Uses of Ether.—Ether may be employed in the form of a spray to induce *local anesthesia* preliminary to opening small abscesses or performing paracentesis, but ethyl chlorid is more effective.

Administered hypodermically (15–30 min.—1.0–2.0 mils), it has long enjoyed a reputation as a diffusible stimulant in *collapse* resulting from poisoning, acute infections, and diseases of the heart itself.

The spirit or compound spirit (Hoffmann's anodyne) may be given in doses of 20 or 30 minims (1.3–2.0 mils) as a carminative in *palpitation of the heart*, due to gastric flatulency, and in *angina pectoris*, when the attack is precipitated by flatulency.

It has been used internally as an anthelmintic against tapeworms and as a carminative in various forms of colic.

To allay its irritant effect on the fauces it is best given in capsules or in ice-water.

CHLOROFORMUM, U. S. P.

(Chloroform, Chloroformum Purificatum, CHCl_3)

Chloroform is a heavy, colorless, non-inflammable liquid, obtained by the action of chlorin on alcohol. It is soluble in two hundred and ten times its volume of water, and miscible with alcohol, oils, and ether. The dose is 3 to 10 minims (0.2–0.6 mil).

PREPARATIONS

DOSE

Aqua Chloroformi, U. S. P.....	1–4 fl. dr. (4.0–15 mils).
Spiritus Chloroformi, U. S. P.....	20–60 min. (1.2–4.0 mils).
Linimentum Chloroformi, U. S. P. (30 per cent. in soap liniment)	

Action.—Chloroform has much the same action as ether. Like the latter, it produces, when freely inhaled, a set of phenomena which may be divided into three stages: The *first stage* is characterized by excitement, reflex effects (coughing, salivation, etc.), mydriasis, irregular breathing, acceleration of the pulse, loss of self-control, muscular rigidity, and impaired sensibility; the *second*, by complete unconsciousness, muscular relaxation, loss of reflexes, moderate contraction of the pupils, regular shallow breathing, fall of blood pressure, and fall of temperature; and the *third*, by symptoms of cardiac and bulbar paralysis—pallor, dilatation of the pupils, feeble irregular breathing, extreme weakness of the pulse, and low temperature.

Circulatory System.—Anesthesia induced by chloroform is always accompanied by a progressive lowering of the blood pressure. This effect is due in part to dilatation of the blood vessels from depression of the vasoconstrictor center, and in part to depression of the heart muscle. Death from chloroform may occur soon after the inhalation has begun from intense reflex stimulation of the inhibitory cardiac center, aided, no doubt, by the weakening effect of the drug on the heart muscle itself. Such sudden arrest of the organ is most likely to occur if the vapor is administered in too concentrated form. Experimentally, it may usually be prevented by division of the vagi or the administration of a large dose of atropin.

Respiratory System.—Chloroform depresses the respiratory center not only directly but also indirectly by lowering the blood pressure in the medulla. The temporary inhibition of respiration that is often observed in the early stage of anesthesia is a reflex phenomenon resulting from the irritant action of the chloroform upon the throat.

Nervous System.—The action of chloroform on the central nervous system is marked by a progressive depression involving successively the cerebrum, the spinal cord and the medulla. As in the case of ether, the sensory neurons appear to be affected before the motor. To maintain anesthesia the inspired air must contain from 1.3 to 1.5 volumes per cent. of the vapor. The fatal concentration is 2 per cent.

Temperature.—In prolonged anesthesia there is a very pronounced fall in the body temperature, due in part to increased loss of heat from dilatation of the cutaneous vessels and in part to decreased production of heat from the absence of muscular movements.

Metabolism.—Chloroform anesthesia increases the output of chlorids, phosphates, sulphates and total nitrogen; it often causes glycosuria and acetonuria, and, if prolonged, it tends to produce fatty changes in the various organs, especially the liver, heart and kidneys.

While acidosis may result from the inhalation of any of the general anesthetics, it is most common from chloroform.

Kidneys.—Light chloroform anesthesia is less likely to cause albuminuria than light ether anesthesia, but deep chloroform narcosis is more injurious to the kidneys than deep ether narcosis, not only in producing irritant effects, but in setting up fatty changes.

Alimentary Canal.—Taken internally in small quantities, chloroform produces a sense of warmth in the stomach, increases peristaltic movements, and aids in the expulsion of flatus.

Local Action.—When applied to the skin, it evaporates rapidly and produces a sense of coldness. When evaporation is prevented, it causes redness of the surface and even vesication.

Lower Organisms.—Even in dilute solution chloroform is destructive to many of the lower forms of animal and vegetable life.

Causes of Death from Chloroform.—Death may occur at three different periods: (1) soon after the inhalation has begun from excessive reflex stimulation of the vagi, aided by direct cardiac depression; (2) during the course of the anesthesia from direct paralysis of the heart and vasomotor center; and (3) in from twelve hours to three or four days after anesthetization, especially after prolonged narcosis, from a toxemia due to degenerative changes in the liver (delayed chloroform-poisoning). This last condition, which is especially common in children and in older persons with diabetes, acidosis or advanced hepatic disease, is characterized by delirium, stupor, coma, and collapse. Incessant vomiting, jaundice and signs of acidosis may also be present.

The Actions of Chloroform and Ether Compared.—

Chloroform is a much more powerful anesthetic than ether. Quantity for quantity, it is more irritating than ether, but being administered in less concentrated form than the latter, it is more agreeable to the patient and is less productive of coughing and choking. The toxic effect of chloroform on the circulation is much greater than that of ether, and the margin of safety between the amount required to induce anesthesia and that which causes death is much narrower with chloroform than with ether. Sudden death from intense vagal stimulation, which is not very rare under chloroform, is never observed under ether. Unpleasant sequelæ (nausea, vomiting, hypersecretion of saliva and bronchial mucus) are more pronounced after ether than chloroform anesthesia; on the other hand, serious metabolic changes (fatty degeneration of the liver, heart, etc.) are much more likely to result from the administration of chloroform than of ether. Finally, the mortality from chloroformization appears to be at least four times that from etherization.

Therapeutics.—Chloroform is employed as a general anesthetic, as a nerve sedative, a carminative, an anthelmintic, and a counterirritant.

General Anesthetic.—The precautions to be observed in administering chloroform as an anesthetic are much the same as those already described in dealing with ether. The vapor, however, must never be concentrated, but well mixed with air. A number of special devices for regulating the strength of the vapor have been recommended, but it is doubtful whether any of these offers any great advantage over the ordinary mask or folded towel in the hands of a skilled anesthetist. If the mask or towel be employed it should not be brought closer to the face than two inches, even after the patient has become accustomed to the anesthetic. If struggling occurs or the breath be held the distance should be increased, as the following inspirations will of necessity be unusually deep. The drug is best delivered drop by drop, at a rate never exceeding 60 drops per minute. Regular snoring breathing, muscular relaxation, and loss of the eye reflexes indicate complete anesthesia. An ordinary operation will not usually require more than an ounce or two of chloroform. The anesthetist should not rely upon any one sign as a warning of danger, but should keep careful watch on the face, the respiration, and the pulse. Lividity of the face, irregular gasping respiration, feebleness of the pulse, or sudden pupillary dilatation (unless accompanied by signs of returning consciousness) call for immediate withdrawal of the anesthetic, lowering of the head, practice of artificial respiration, rhythmic compression of the

precordia (40 times a minute) and the hypodermic administration of circulatory stimulants, such as ammonia, caffeine, and strychnin. The use of epinephrin is inadvisable (see p. 62). Massage of the heart through the diaphragm, when operating on the abdomen, has been recommended. In sudden arrest of the heart from excessive inhibition at the beginning of anesthesia, the injection of atropin in large dose should be included among the restorative measures.

When chloroform is administered in the presence of lighted gas-jets, the room should be well ventilated, since the burnt vapor of the anesthetic yields irritant products (especially carbonyl chlorid) capable of inducing pneumonia when inhaled in concentrated form.

Conditions Favoring the Use of Chloroform as an Anesthetic.—While chloroform is ordinarily more dangerous than ether, it is to be preferred to the latter when the patient is suffering from an acute inflammation of the respiratory tract; when it is desired merely to lessen the excitability of the nervous system, as in checking convulsions, or to dull intense pain, as in labor or biliary colic; when very complete muscular relaxation is required, as in the reduction of certain luxations; and when the actual cautery is to be applied to the mouth or about the face.

In very hot climates chloroform is usually preferred to ether, because the latter is so very volatile that there is difficulty in maintaining complete anesthesia with it, at least when open methods are used. In military practice, also, chloroform is preferable on account of the rapidity of its action and the small quantity required to induce insensibility.

Contraindications to Chloroform Anesthesia.—Chloroform is particularly to be avoided in all conditions of circulatory weakness; in all operations likely to be attended by profuse hemorrhage; in operations requiring the sitting posture; in very prolonged operations; in conditions which favor acidosis (diabetes, starvation, eclampsia, sepsis, etc), in serious hepatic disease, and in the status lymphaticus.

Nerve-sedative.—A few whiffs of chloroform may be employed to allay motor excitation in *strychnin-poisoning*, *tetanus*, and *chorea insaniens*, and to allay local spasm in *asthma*, *whooping cough*, and severe attacks of *renal* and *biliary colic*.

In attacks of *angina pectoris* of great intensity Balfour and Osler recommend inhalations of chloroform. It may be dropped upon a handkerchief, or, as Balfour recommends, poured on a sponge in a smelling-bottle, and the patient told to breathe it through the nose. It should never be used if the bloodpressure is low and symptoms of shock accompany the pain.

In the obstinate cough of *pulmonary tuberculosis* the addition of chloroform to the usual cough-mixture is often advantageous.

- ℞. Codeinæ sulphatis..... gr. iv. (0.26 gm.)
 Acidi hydrocyanici diluti..... ℥ xl (2.5 mils)
 Spiritus chloroformi..... f ℥ ij (8.0 mils)
 Glycerini..... f ℥ ss (15.0 mils)
 Elixir aurantii..... q. s. ad f ℥ iij (90.0 mils).—M.
 Dose.—One teaspoonful.

Carminative.—It is a useful carminative and sedative in *gastralgia* and *intestinal colic*. The following combination will be found useful in *gastralgia*:

- ℞. Chloroformi..... f ℥ iss-ij (5.5–8.0 mils)
 Spiritus ammoniæ aromatici,
 Spiritus vini gallici,
 Tincturæ cardamomi compositæ, āā f ℥ v (18.0 mils).—M.

Sig.—A teaspoonful in hot water every fifteen or thirty minutes until relief is obtained.

Anthelmintic.—It has been used in large doses (f ℥ ss-j—2.0–4.0 mils) as an anthelmintic against *tapeworms*, but it is an unreliable remedy. In nineteen cases reported by Whyte and Leichtenstern it proved successful in only two instances.

Counterirritant.—In the form of a liniment chloroform is extensively used as a stimulating application in *myalgia*, *rheumatoid arthritis*, *sprains*, and *contusions*. Methyl salicylate may often be added to it with advantage, as in the following formula:

- ℞. Methylis salicylatis..... f ℥ i (30.0 mils)
 Linimenti chloroformi..... q. s. ad f ℥ vi (180.0 mils).—M.
 Sig.—Apply several times a day.

NITROGEN MONOXID

(Nitrous Oxid, Laughing Gas, N_2O)

Nitrogen monoxid is obtained from the distillation of ammonium nitrate, and appears as a colorless, odorless gas having a somewhat sweetish taste. By pressure it is converted into a liquid, and in this form it is stored in steel cylinders for future use.

Pharmacologic Action.—When freely inhaled, undiluted nitrogen monoxid causes an increase of blood pressure, quickened respiration, exhilaration, ringing in the ears, marked lividity of the face, and in a minute or two complete unconsciousness. Upon withdrawal of the anesthetic recovery ensues in from thirty to sixty seconds. Anesthesia thus induced is caused partly by the specific action of the gas on the cerebrum and partly by asphyxia resulting from the exclusion of oxygen. The gas has no direct effect on the heart or medullary centers, the increased

blood pressure being due to asphyxia. For short operations, such as pulling teeth, opening abscesses, etc., it is the safest of the general anesthetics, and, moreover, its use is not followed by unpleasant after-effects. Hewitt was able to find records of but 17 deaths from its administration between the years 1860 and 1900.

By diluting nitrous oxid with a sufficient amount of oxygen (15 to 20 per cent.) to prevent asphyxia, narcosis can be produced in a minute or two, and maintained almost indefinitely. Anesthesia lasting an hour requires on an average about 150 gallons of nitrous oxid gas. The advantages of nitrous oxid-oxygen anesthesia are the absence of odor, the rapidity of action, and the minimal after-effects; the disadvantages are the cumbersome character of the apparatus required, the relatively high cost of the gas, and the absence of complete muscular relaxation. Nitrous oxid-oxygen anesthesia is contraindicated in persons with advanced arterial degeneration, and is often ineffective in young children, persons with extremely nervous temperaments, athletes, and alcoholic subjects. To secure the requisite degree of anesthesia and of muscular relaxation it is sometimes safer to use less nitrous oxid and to add a little ether (2 to 8 per cent.) to the combination. The administration of morphin and scopolamin also increases the efficiency of nitrous oxid, but not without adding somewhat to its danger. In the hands of an expert anesthetist nitrous oxid-oxygen is apparently as safe as ether, but in inexperienced hands it is much more dangerous than ether.

ÆTHYLIS CHLORIDUM, U. S. P.

(Ethyl Chlorid, C_2H_5Cl)

Ethyl chlorid is prepared by the action of hydrochloric acid upon absolute alcohol, the hydroxyl group in the latter being replaced by chlorin. Under pressure or at a low temperature it is a colorless, highly volatile liquid, having an odor resembling that of chloroform and a burning taste. As its vapor is very inflammable, it should not be used in proximity to a gas-flame or fire. It is dispensed in sealed glass or metal tubes, provided with a cap and when the latter is removed it escapes in the form of a fine spray.

Pharmacologic Action and Therapeutics.—Ethyl chlorid is a fugacious general anesthetic. Accompanying the anesthesia there is a fall in the arterial pressure, due probably to direct cardiac action. The vapor is best administered from a special mask, which restricts the admission of air. Anesthesia is produced in from one to three minutes, from 1 to 2 fluidrams (4.0–

8.0 mils) of the drug being required for the purpose. Upon removal of the mask recovery ensues almost at once.

As a general anesthetic, ethyl chlorid is only suitable for *short surgical operations* and as a *preliminary to ether anesthesia*, although it has been used to some extent for operations lasting half an hour or longer. Its action is rapid, is not attended by irritation of the respiratory passages, choking sensation, cough, or cyanosis, and is not often followed by nausea or vomiting; but, on the other hand, it does not result in complete muscular relaxation. Ethyl chlorid has an advantage over nitrous oxid in not requiring cumbersome apparatus for its administration, but it is decidedly more dangerous, the mortality rate from its use being not much below that of chloroform.

When sprayed upon the skin, ethyl chlorid evaporates so rapidly that it freezes the tissues and so renders them insensitive. The anesthesia is due partly to the cold and partly to the anemia. Sloughing may result if the freezing is too long continued. Local anesthesia by ethyl chlorid is often employed in *minor operations* requiring but a single incision or puncture, such as opening abscesses, aspirating pleural or abdominal effusions.

ÆTHYLIS BROMIDUM

(Ethyl Bromid, Hydrobromic Ether, C_2H_5Br)

Ethyl bromid is obtained by the distillation of a mixture of ethyl alcohol, sulphuric acid, and potassium bromid. When perfectly pure it forms a colorless, highly volatile, inflammable liquid having a sweetish taste and a chloroformic odor. On exposure to air it liberates bromin and hydrobromic acid and becomes unfit for use. It should be kept in dark amber-colored, well-stoppered bottles. It must not be confused with the poisonous *ethylene bromid*.

Ethyl bromid has an action similar to that of ethyl chlorid, but as it readily undergoes decomposition, as it is more dangerous than ethyl chlorid, and as its administration imparts an unpleasant garlicky odor to the breath lasting for 24 hours or longer, it is rarely, or never, employed as an anesthetic at the present time.

INTOXICANTS

ALCOHOL, U. S. P.

(Ethyl Alcohol, Grain Alcohol, C_2H_5OH)

Ethyl alcohol is formed from saccharine material by yeast fermentation. The official preparation contains 92.3 per cent. by

weight of absolute ethyl alcohol, and appears as a colorless, inflammable liquid, having a pungent odor and a burning taste.

PREPARATIONS

Alcohol Dehydratum, U. S. P. (99 per cent. alcohol)

Alcohol Dilutum, U. S. P. (41 to 42 per cent. alcohol)

ALCOHOLIC BEVERAGES

Spirits:

Whiskey (Spiritus Frumenti)—44 to 55 per cent. by volume of alcohol; distilled from fermented grain.

Brandy or Cognac (Spiritus Vini Gallici)—44 to 55 per cent. by volume of alcohol; distilled from fermented grape-juice.

Gin—about 60 per cent. of alcohol with oil of juniper; distilled from fermented grain and redistilled with juniper berries.

Rum—50 to 60 per cent. of alcohol; distilled from fermented molasses.

Wines:

Red wine (Claret, Bordeaux)—10 to 15 per cent. of alcohol with tannin; prepared by fermenting the juice of red grapes in the presence of their skins.

White wine (Sauterne, Chablis, etc.)—10 to 15 per cent. of alcohol and no tannin; prepared by fermenting grapes that have been freed from skins, seeds and stems.

Champagne—10 to 15 per cent. of alcohol with CO₂ and sugar.

Sherry (Vinum Xericum)—15 to 20 per cent. of alcohol with tartaric acid, acetic acid and other fatty acids, but no sugar.

Port (Vinum Portense)—15 to 20 per cent. of alcohol with acids and sugar.

Malt Liquors:

Ale	} Contain from 3 to 6 per cent. of alcohol with CO ₂ , sugars, fatty acids, and a bitter principle (hops); prepared by fermenting an infusion of malt (germinated barley).
Beer	
Porter	
Stout	

Elixirs are aromatic, sweetened, hydro-alcoholic liquids containing sugar, various flavoring agents, and a large percentage of alcohol. The so-called "liquers," "cordials," "crèmes," etc. (Chartreuse, Crème de menthe, Benedictine Absinthe, Curaçao), which belong in this group, contain about 33 per cent. of sugar and from 50 to 65 per cent. by volume of alcohol.

Two elixirs are official: Elixir Aromaticum, the flavoring principle of which is orange, and Elixir Glycyrrhizæ. These are used as vehicles for drugs with an unpleasant taste.

Denatured Alcohol.—This term is applied to ethyl alcohol to which have been added from 2 to 10 per cent. of methyl (wood) alcohol and 0.5 per cent. of benzine or of pyridin bases to make it unfit for consumption. It is not suitable for either internal or external use.

Pharmacologic Action.—Circulatory System.—Moderate doses of alcohol cause acceleration of the pulse and flushing of the surface, without materially augmenting the blood pressure. The acceleration of the pulse is due (1) in part to excitement, (2) in part to reflex stimulation from gastric irritation, and

probably also (3) in part to a direct action, slight and transitory, on the nervous or muscular mechanism of the heart itself. The flushing of the surface is caused by dilatation of the peripheral vessels from depression of the vasoconstrictor center. The vessels of the splanchnic area apparently do not share in the dilatation; indeed, there is reason to believe that they are somewhat constricted.

While alcohol increases the amount of blood pumped by the heart in a given length of time (Wood and Hoyt), it does not cause under ordinary conditions any material change in the blood pressure, probably because the actions of the drug in increasing the heart power and in dilating the peripheral vessels are about equally balanced. It is generally recognized, however, that large amounts of alcohol cause a notable fall in arterial pressure through depression of both the vasoconstrictor center and the heart muscle.

Nervous System.—The first effect of alcohol upon the nervous system is one of apparent stimulation, with indications of increased mental and motor activity. As a matter of fact, however, attention, judgment, self-control, and the higher mental processes generally, as well as the capacity for physical work, are distinctly impaired at once, even by small quantities of the drug, and, therefore, the vivacity of speech and excess of motor energy often displayed in the early stage of alcoholic intoxication must be attributed to a depression of the inhibitory or controlling functions rather than to a true stimulation of the mental faculties.

With large doses of alcohol the stage of excitement is soon followed by one of depression, which is characterized by impairment of memory, thick speech, ataxia, lessened reflex irritability and somnolence, gradually deepening into stupor and coma.

Respiration.—Moderate amounts of alcohol quicken the respiration and increase the volume of air inhaled. These effects are due in part to reflex stimulation of the respiratory center by gastric irritation and probably also in part to a direct stimulation of the center, for other irritants when taken by the mouth affect the respiration much less than alcohol and the effects occur almost immediately when the drug is injected into the carotid artery. Toxic doses of alcohol depress the respiratory center.

Alimentary Canal.—An agreeable preparation of alcohol, if taken before meals in small quantities, often acts favorably on digestion. It whets the appetite and thus *indirectly* excites a flow of gastric juice (cephalogenous secretion). It also accelerates the action of the peptic ferments, promotes absorption, and probably increases the motor activity of the stomach. Concen-

trations of 10 to 15 per cent. have probably no *direct* influence on gastric secretion (endogenous secretion), but concentrations above 15 per cent. while in the stomach retard the secretion of gastric juice, increase the secretion of mucus and depress peptic digestion. Apart from any influence exerted by their alcoholic content, beer may act unfavorably on digestion because of its extractives and red wine because of its tannin. Alcohol in concentrated form, especially if taken on an empty stomach, acts as an irritant and tends to produce gastritis. In moderate amounts alcohol does not directly influence intestinal digestion, as very little of the drug enters the bowel. *In vitro*, however, even small quantities strongly depress the action of the pancreatic ferments.

After absorption, alcohol, even when administered by the rectum, produces a flow of gastric juice which is rich in hydrochloric acid and probably stimulates also the pancreatic secretion. According to Salant, alcohol by the mouth markedly increases the secretion of bile.

Metabolism.—In moderate amounts alcohol is almost completely burned in the body, spares to a certain extent the destruction of fats and proteins, supplies energy to the tissues, and serves to maintain the body-weight, when, for any reason, the diet is insufficient. To this extent alcohol is a food. It is far from being a perfect food, however, for it is less economically utilized than other food-stuffs, it cannot be stored up as a reserve to be drawn upon in time of need, and, above all, it has important toxic side-actions. Despite these drawbacks, alcohol may sometimes be advantageously employed when other less readily utilized foods may not be given, as in exhausting febrile diseases and advanced diabetes.

Temperature.—Alcohol lowers the body-temperature to a slight extent both by dilating the cutaneous vessels and by increasing the secretion of sweat. Accompanying the fall of temperature a sensation of warmth is experienced, which is also due to the increased amount of blood in the skin.

Excretion.—Alcohol is almost completely oxidized in the body, only a small amount (usually less than 2 or 3 per cent.) being excreted by the kidneys and lungs. The products of its combustion are carbon dioxid and water.

Local Action.—In concentrated form alcohol abstracts water from the cells and precipitates the proteins, and thus causes decided irritation. When applied to the skin in dilute form and allowed to evaporate it produces a cooling effect.

Action on Lower Organisms.—Alcohol has moderate germicidal power. According to Harrington and others, the best results are obtained with alcohol of 60 per cent. strength, germicidal power

of the drug diminishing with departures in either direction from this dilution.

Toxicology.—Acute Poisoning.—The ingestion of a large quantity of alcohol first causes apparent stimulation, with flushing of the face, quickened breathing and pulse, motor restlessness, impulsiveness, exaggerated talkativeness, a sense of well being, and a deceptive feeling of increased strength and capability. Within an hour, or in much shorter time if a very large dose has been taken on an empty stomach or if the person has not been accustomed to the use of alcohol, the functions of the central nervous system become definitely depressed, as shown by mental confusion, thick muttering speech, uncertain gait, general muscular relaxation and drowsiness. In some cases before the occurrence of sopor the abolition of emotional restraint results in maniacal excitement, but usually the patient is only merry and silly. Retching and vomiting may also occur. Gradually the drowsiness deepens into sleep, and then, if the intoxication is sufficiently severe, coma and symptoms of medullary depression supervene, this stage being characterized by dilatation of the pupils, slow and stertorous breathing, feeble pulse, clammy skin, subnormal temperature, abolition of most of the reflexes and sometimes relaxation of the sphincters. Occasionally, the coma is interrupted by convulsions.

Recovery is the rule, but death may occur within a few hours from respiratory paralysis, cardiac failure, or pulmonary edema. With the return of consciousness, symptoms of gastric irritation—anorexia, coated tongue, nausea and vomiting—develop, with depression, headache, and general muscular soreness (“Katzenjammer”). Alcoholic coma must be distinguished from coma due to apoplexy, uremia, diabetes, cranial injuries, epilepsy, thermic fever, opium-poisoning, etc.

Treatment.—The stomach should be emptied by the stomach-pump or a hypodermic injection of apomorphin ($\frac{1}{8}$ gr.—0.008 gm.). Catheterization may be required. In case of threatened collapse recourse must be had to external heat, enemas of hot saline solution, and subcutaneous injections of caffein, strychnin and atropin. The subsequent headache, nervousness and gastric irritability are best relieved by a laxative dose of calomel, with the administration of sodium bicarbonate and bismuth subcarbonate before meals, and a bromid with caffein or a bromid with acetphenetidin after meals.

Chronic Poisoning.—The effects of the habitual use of alcohol in excess are due in part to the irritant action of the intoxicant and in part to its specific action on the nervous system. It is not unlikely, however, that some of the changes occurring in the

viscera depend less upon the alcohol itself than upon secondary toxic products resulting from indigestion and faulty metabolism. The lesions in the alimentary canal are of an inflammatory character, while those in the liver, kidneys, heart, muscles and nerves are essentially degenerative.

The most common manifestations of chronic alcoholism are injection of the conjunctivæ, redness of the face, particularly of the nose, the usual phenomena of chronic gastro-enteritis, tremor of the fingers, tongue and lips, muscular weakness, dulling of the mental faculties and deterioration of the morals. The general nutrition is often disturbed, some patients becoming more or less emaciated, others obese. Enlargement of the liver, in consequence of fatty changes, is a common occurrence and in some cases (5 to 6 per cent. of alcoholics), especially in spirit drinkers, symptoms of atrophic cirrhosis of the liver eventually develop. In many instances the kidneys become the seat of cirrhotic and catarrhal changes. The occurrence of arteriosclerosis and of chronic myocardial disease seems also to be favored by chronic alcoholism. A marked hypertrophy of the heart is not rarely seen in men who consume large quantities of beer and do very heavy work. Amblyopia, due to orbital optic neuritis, sometimes develops.

Of the nervous affections resulting from chronic alcoholism, polyneuritis is especially frequent; indeed alcoholism is the commonest cause of the toxic form of this disease. Proportionately more women are affected than men. In many cases the neuritic features are accompanied by a peculiar mental disturbance characterized by a loss of memory for recent events, lack of power of attention, fabrications, and disorientation as regards time and place (Korsakow's psychosis). The outcome in most cases is favorable, but permanent dementia may supervene. Not rarely the prolonged use of alcohol leads gradually to definite insanity. This may manifest itself by simple progressive weakening of the mind, with episodic and transitory hallucinations and delusions, or it may take the form of a maniacal psychosis or of a paranoid dementia with more or less systematized delusions of a depressive or persecutory character. The lesions found most frequently in association with alcoholic insanity are hemorrhagic pachymeningitis, chronic leptomeningitis, and serous effusion into the ventricles. Microscopic examination reveals degenerative changes in the cortical cells and fibers.

Epileptic convulsions occasionally occur in the course of alcoholic psychoses or as isolated phenomena.

Effect of Chronic Alcoholism on Offspring.—Statistics indicate a much larger proportion of cases of deficient vitality, insanity,

epilepsy, criminality and alcoholism among the children of alcoholics than among the descendants of total abstainers, but it is not definitely known whether the danger of alcoholic parents lies in the effect of the alcohol itself upon the germ-plasm or the fetal blood, or whether it lies in the transmission of the hereditary degeneracy which led to the inebriety of the parent or parents. Drunkenness in several generations of the same family may be the result of several factors, and it goes on until regression to the normal by conjugation with a healthy stock occurs, or terminates by degeneration and elimination of the stock (Mott).

Treatment of Chronic Alcoholism.—The patient is best treated in a special hospital or sanatorium, as he rarely has sufficient will power of his own to abstain from drink. The alcohol should be withdrawn as rapidly as possible, usually within two or three days. Highly seasoned nutritious food should be given at frequent intervals. Robust patients are often benefited by warm baths (103° F.), for ten or fifteen minutes, followed by cold sponging. Cathartics are almost always indicated and should be given freely. Violent outbreaks the result of acute intoxication may often be subdued by a hypodermic injection of apomorphin, which has a sedative as well as an emetic action. Stomachics, such as nux vomica, capsicum and ginger, are frequently of service when given with food. Atropin hypodermically, ($\frac{1}{120}$ gr.—0.0005 gm.), two or three times a day, is sometimes useful in controlling nervousness. Intramuscular injections of ergot have also been highly recommended. Sleep is best procured by chloral (15–20 gr.—1.0–1.3 gm.), paraldehyd (1 dram—4.0 mls), repeated every hour, if necessary for two or three doses, or scopolamin hydrobromid ($\frac{1}{100}$ gr.—0.00065 gm.). The mixture of morphin $\frac{1}{8}$ gr. (0.008 gm.); chloral, 20 grains (1.3 gm.); tincture of hyoscyamus, $\frac{1}{2}$ dram (2.0 mls); tincture of capsicum 3 minims (0.2 mil); and water $\frac{1}{2}$ ounce (15 mls), recommended by Lambert, is often effective.

Strong moral support, the creation of suitable surroundings, mental diversion, abundant exercise in the open air, and a varied diet of wholesome food are the most effective means of keeping the patient from the use of alcohol. The prospects of permanent cure are better than with morphin or cocain. Relapse, however, is extremely common.

Delirium Tremens (Mania à Potu).—Delirium tremens is an acute psychosis occurring in the course of chronic alcoholism. It is observed chiefly in drinkers of distilled spirits. The exciting cause is often found in the sudden withdrawal of alcohol, a debauch, abstinence from food, overexertion, psychic shock, trauma, a surgical operation or an acute infection, especially

pneumonia. The pathogenesis of the condition is not known. Cerebral edema is often found at necropsy, but apparently this is a late or secondary feature.

Two well-defined stages of delirium tremens may be recognized: a premonitory stage, characterized by insomnia, restlessness, tremors, apprehensiveness and occasionally poorly formed hallucinations; and a second stage characterized by widespread tremor, persistent insomnia, talkative delirium, and definite hallucinations of a terrifying character, usually of sight, but sometimes of hearing. The pulse is rapid and often weak, the skin is moist, the face is usually flushed, but it may be pale, and the temperature, even in the absence of pneumonia, is not rarely elevated a degree or two. In many cases, under appropriate treatment, the process does not continue beyond the premonitory stage, but terminates favorably in the course of two or three days. The second stage lasts, as a rule, two or three days and ends in recovery or in death. Convalescence often follows a prolonged sleep. In about 10 per cent. of the cases stupor succeeds the delirium and symptoms of the so-called typhoid state supervene. Meningitic phenomena, such as general hyperesthesia, rigidity of the neck, exaggeration of the deep reflexes, etc., may also develop. This condition, which has been shown to be associated with an excessive accumulation of serous fluid in the pia-arachnoid space ("wet brain"), may persist for several weeks. The mortality in delirium tremens varies with the stage during which treatment is instituted and the presence or absence of complications. It averages about 10 per cent., and after the occurrence of well-defined hallucinations it is not less than 25 or 30 per cent. In cases advanced to the stage of cerebral edema the mortality is about 80 per cent. Death is usually due to pneumonia, but it may be the result of primary cardiac failure.

Treatment.—In the first stage the important indications are to support the system by means of nourishing food, to favor elimination through the administration of a quickly acting cathartic and the free use of water, and to secure sleep by giving bromids in doses of 1 dram (4.0 gm.) every three or four hours or of trional in doses of 20 grains (1.3 gm.), in hot milk or broth, every fourth hour, care being exercised not to overdo the exhibition of narcotics. Alcohol in moderate doses is undoubtedly of value at this period, although many writers recommend its withdrawal from the first. Cool packs in sthenic cases and warm baths in asthenic cases are helpful. Spinal drainage is sometimes of service, but, as a rule, it is more effective in the second stage.

In the second stage rest in bed is essential. Physical restraint is almost always required and may be secured by folded sheets drawn across the body and tied to the bed and by the use of wrist- and ankle-straps. An abundance of nourishment, in the form of milk, milk and eggs, and highly seasoned broths with eggs beaten into them just as they have ceased boiling, is necessary. In uncomplicated cases alcohol is better avoided in this stage. Somnifacients are much less effective than in incipient cases, but bromids, chloral, paraldehyd or trional should be used. Morphin should be given sparingly, if at all. Lambert speaks favorably of a combination of strychnin ($\frac{1}{30}$ gr.—0.002 gm.), hyoscin sulphate ($\frac{1}{100}$ gr.—0.0006 gm.), and apomorphin hydrochlorid ($\frac{1}{10}$ gr.—0.006 gm.). In robust patients cold affusions, followed by vigorous rubbing, are sometimes of aid in producing sleep. Spinal drainage is often advisable. For circulatory weakness the most efficient remedies are digitalis, strychnin and atropin.

Alcoholic wet brain is best treated by giving highly nutritious liquids, using the nasal tube, if necessary; by securing free evacuation of the bowels; by withdrawing fluid from the spinal canal; by administering circulatory stimulants (digitalis, caffen, atropin, strychnin) hypodermically; and by applying blisters or other counterirritant agents to the back of the neck.

Therapeutics.—Alcohol is used internally as a quickly acting circulatory stimulant, a stomachic, a mild narcotic or somnifacient, an auxiliary food, and a counteractive of the local effects of phenol. Externally, it is employed as an antiseptic, a cooling application, an astringent, and an antihydrotic.

Alcohol is useful as a quickly acting circulatory stimulant in various forms of acute heart failure, such as occurs in *syncope* and in many forms of *poisoning*. In traumatic shock, with persistent low blood pressure, it is likely to prove harmful. As a stomachic, in the form of a light wine or diluted spirits, it is sometimes beneficial in *simple atony of the stomach* occurring during convalescence from acute illness, resulting from overwork, or appearing as a senile phenomenon, although the danger of inducing chronic alcoholism must always be borne in mind. In mild forms of *insomnia* alcohol, in the form of beer or well diluted whiskey, may also be of service, but much prudence must be exercised in prescribing it. In *exhausting infections*, especially typhoid fever and septicemia, when the heart is weak and toxic features are pronounced, its reputation as a restorative is well deserved. In such cases it serves as a stomachic, a readily absorbed food, and a narcotic. Beginning with 2 drams (8.0 mls) of whiskey every three hours, the amount may be gradually

increased to 4 or even 6 ounces (120.0—180.0 mls) a day. Brunton's rule for testing its efficacy is a good one: "Sit by the side of your patient for a while and watch him after the administration of a dose of alcohol, and if you find that the alcohol brings back the various functions nearer to the normal, then it is doing good; if the functions of the organs diverge further from the normal after the administration of alcohol, then it is doing harm."

During the fasting treatment of *diabetes mellitus* one or two ounces (30.0—60.0 mls) of a whiskey a day may be allowed to replace carbohydrates, to spare the proteins, and to lessen the tissue waste.

As alcohol has greater solvent affinity for phenol than for the fluids of the tissues, it may be used to prevent the penetration of phenol and to lessen its local effects. In *internal phenol poisoning* three or four ounces (90.0—120.0 mls) of whiskey or of 20 per cent. alcohol should be introduced into the stomach and immediately washed out with warm water. Under no circumstances should the mixture be allowed to remain in the stomach, as the alcohol favors absorption of the phenol.

External Uses.—Bathing with alcohol is a useful adjuvant to other measures in *disinfecting the skin*. A mixture of alcohol and water makes a useful evaporating lotion in the treatment of *contusions* with ecchymosis. Applied to small wounds, it is also effective in controlling *capillary oozing*. Sponging the body with alcohol and water is often serviceable in checking the *night-sweats* of tuberculosis. In prolonged illness bathing all parts exposed to pressure once or twice daily with alcohol serves to harden the skin and to *prevent bedsores*.

The injection of alcohol (80–90 per cent.) into the second and third divisions of the nerve near the foramina of exit from the skull has given good results in *trigeminal neuralgia*. The injection does not effect a permanent cure, but, by bringing about degenerative changes in the nerve, it usually gives complete relief for an average period of from eight months to a year.

Contraindications.—Inflammatory or ulcerative conditions of digestive tract, hyperchlorhydria, urethritis, and gout are important contraindications to the internal use of alcohol. It is never justifiable to prescribe alcoholic beverages for persons of unstable nervous system or persons who have once been addicted to the use of alcohol and who have broken the habit.

METHYL ALCOHOL

(Wood Alcohol, Columbian Spirits, CH_3OH)

Methyl alcohol is extensively employed in the arts and is of interest to the physician because of the many cases of poisoning

that have resulted from its use as an adulterant of whiskey and other alcoholic beverages and of cologne-water, bay-rum, etc. Its actions resemble those of ethyl alcohol, but it is excreted more slowly and is imperfectly oxidized, formic acid being the chief product of its incomplete combustion. The formic acid is rapidly eliminated by the kidneys, but gives rise to acidosis. Methyl alcohol has often proved toxic when used externally, and even the vapor of it is dangerous when ventilation is insufficient. Poisoning is much more likely to result in death than that from ethyl alcohol.

Symptoms of Poisoning.—The symptoms resemble those of ordinary alcoholic intoxication, the chief differences being the protracted coma, which sometimes lasts two or three days, and the more serious after-effects, particularly partial or complete blindness from destructive inflammation of the optic nerve or retina, which occurs in about one-half of all cases. The primary symptoms consist of abdominal pain, nausea and vomiting, headache, vertigo, and disturbance of vision. Later, restlessness, delirium, coma and collapse occur. The pupils are dilated and insensitive. Dyspnea is often marked. Death from respiratory paralysis may occur in from a few hours to two or three days. Occasionally the symptoms are deferred for several days and then prove rapidly fatal.

Wood and Buller found 153 cases of blindness and 122 deaths recorded up to 1904, and since then a great many additional cases have been reported. In December, 1911, 89 deaths and 5 cases of total blindness due to the use of a cheap drink containing wood alcohol occurred in a Berlin lodging house (Stadelmann).

Treatment.—This consists of rapid evacuation of the stomach, purging, administration of respiratory and circulatory stimulants, proctoclysis with a solution of sodium bicarbonate, and, if necessary, intravenous injection of normal saline solution.

ANTISPASMODICS

Antispasmodics are remedies used to control minor grades of motor excitation and to lessen states of general nervous irritability. They vary in the manner of their action. Some, such as hops and lactucarium, are feeble depressants of the nervous system, while others, such as asafetida and valerian, probably owe much of their efficacy to the mental effect induced by their strong odor and taste. As a class, antispasmodics are chiefly useful in hysteria and allied conditions. The following drugs are the most important members of this group:

Camphor	Cimicifuga
Asafetida	Lactucarium
Valerian	Hops
Compound spirit of ether	Sumbul
Musk	Viburnum prunifolium.

CAMPHORA, U. S. P.

(Camphor, $C_9H_{16}CO$)

Camphor is a stearopten obtained by distilling the wood of the camphor tree—*Cinnamomum Camphora*—growing in China and Japan. It is also prepared synthetically. It is a whitish, translucent volatile substance, having a penetrating odor and a pungent taste. It dissolves readily in all ordinary menstrua, except water, in which it is only sparingly soluble. With chloral hydrate, thymol, menthol and salol it liquefies without undergoing any chemical change. The dose is from 1 to 5 grains (0.06–0.3 gm.).

PREPARATIONS

DOSE

Aqua Camphoræ, U. S. P. (0.8 per cent.).....	1–4 fl. dr. (4.0–15.0 mls)
Spiritus Camphoræ, U. S. P. (10 per cent.).....	10–30 min. (0.6–2.0 mls)
Linimentum Camphoræ, U. S. P. (20 per cent. in cottonseed oil)	
Linimentum Belladonnæ, U. S. P. (5 per cent. in flex. of belladonna)	
Linimentum Chloroformi, U. S. P. (about 3 per cent.)	
Linimentum Saponis, U. S. P. (4.5 per cent.)	

It also enters into *Tinctura opii camphorata*.

Pharmacologic Action.—Externally, camphor is a mild rubefacient and analgesic. It is also a feeble antiseptic. In full therapeutic doses it apparently stimulates the controlling centers of the cerebrum and thus tends to overcome nervous instability. It is also said to be anaphrodisiac. Clinically, it exerts a stimulating effect upon the heart, but in animal experimentation this action cannot be demonstrated with certainty. In the stomach it acts as a carminative, inducing a sensation of warmth, increasing peristalsis, and aiding in the expulsion of flatus. It is readily absorbed from the digestive tract and subcutaneous tissue, and is eliminated chiefly by the kidneys in combination with glycuronic acid.

Toxic doses first produce excitement, nausea and vomiting, delirium and epileptiform convulsions, and then coma and collapse.

Therapeutics.—Camphor is employed as an antispasmodic, circulatory stimulant, carminative, rubefacient and antipruritic. As an antispasmodic it has been extensively used in *hysteria* and allied conditions and in the *climacteric neuroses*.

As a circulatory stimulant it is of value, if given subcutaneously or intramuscularly, in impending heart failure, especially when this is due to *acute infections*, such as *pneumonia*, *typhoid fever*, or *septicemia*, or to *poisoning by chloral*, *muscarin*, or other drugs that directly depress the cardiac muscle. As a carminative camphor is often of service in *gastric flatulence*, *colic* and *serous diarrhea*. As a rubefacient it is much used in the form of a liniment in *sprains*, *bruises*, and *myalgia*. In the form of chloral-camphor or menthol-camphor it is sometimes efficacious as a local remedy in *toothache* and *neuralgia*. Anderson's powder is a useful antipruritic dusting-powder in *simple erythema*, *intertrigo*, *urticaria*, etc. It consists of 1 to 2 drams (4.0–8.0 gm.) of finely pulverized camphor to $\frac{1}{2}$ ounce (15.0 gm.) each of powdered starch and zinc oxid.

Camphor is also a useful remedy in *acute coryza*, particularly when given early in the attack. It may be used internally and also by inhalation, a teaspoonful of powdered camphor being added to a tumblerful of boiling water, and the fumes inhaled.

Administration.—Camphor may be given by the mouth in the form of the water or spirit, or in substance in pill or capsule. As a circulatory stimulant, however, it is of service only when given subcutaneously or intramuscularly. From 1 to 2 grains (0.06–0.13 gm.) may be dissolved in 15 minims (1.0 mil) of sterile olive oil, and injected every three hours, or even every two hours, if the symptoms are very urgent. In *coryza* the following combination may be employed:

R.	Codeinæ sulphatis.....	gr. iiss (0.16 gm.)
	Pulveris camphoræ.....	gr. xx (1.3 gm.)
	Extracti belladonnæ.....	gr. iss (0.1 gm.)
	Ammonii carbonatis.	
	Terpini hydratis.....	āā gr. xl (2.5 gm.).—M.
	Pone in capsulas No. xx.	
	Sig.—One every two or three hours.	

Camphora Monobromata, U. S. P. (Monobromated Camphor; $C_{10}H_{15}Br.CO$).—This preparation is obtained from the union of bromin and camphor in the presence of heat, and occurs as colorless prismatic needles or scales, having a mild camphoraceous odor and taste. It is very sparingly soluble in water or glycerin, but freely soluble in alcohol, ether, or chloroform. The dose is from 2 to 5 grains (0.13–0.3 gm.) in pill or capsule.

Monobromated camphor is especially useful as an anaphrodisiac in *abnormal sexual excitement*, *chordee*, *spermatorrhea*, etc. Its chief drawback is its tendency to induce heartburn and eructations. It has also been used to some extent as a substitute for

the bromids in *minor epilepsy* (*petit mal*). As an anaphrodisiac it may be combined with scopolamin (hyoscin), as in the following formula:

R_x. Scopolaminæ hydrobromidi..... gr. $\frac{1}{10}$ (0.006 gm.)
 Camphoræ monobromatæ..... ʒj (4.0 gm.).—M.
 Pone in capsulas No. xx.
 Sig.—One capsule at bedtime.

Acidum camphoricum (camphoric acid) is employed chiefly as an anhydrotic (see p. 278).

ASAFÆTIDA, U. S. P.

(Asafetida)

Asafetida is a gum-resin obtained by incising the roots of *Ferula fætida*, an umbelliferous plant abounding in Persia and Afghanistan. It appears in the form of irregular masses or tears of a yellowish-brown color, and has a persistent garlicky odor and an acrid taste. It consists of gum, resin, and an essential oil (about 4 per cent.), which is rich in sulphur. The oil is the most active ingredient. The dose is from 1 to 10 grains (0.06–0.65 gm.).

PREPARATIONS

DOSE

Emulsum Asafætida, U. S. P. (4 per cent. watery emulsion).....	1–4 fl. dr. (4.0–15.0 mls)
Tinctura Asafætida, U. S. P.....	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls)
Pilulæ Asafætida, U. S. P. (3 gr.–0.2 gm.).....	1–3 pills

Therapeutics.—Asafetida is employed chiefly as an antispasmodic and carminative. As an antispasmodic it is used in *hysteria* and *other states of nervous instability*. As a carminative the drug is an excellent remedy in *infantile colic* and the *flatulent dyspepsia of the aged*. The chief drawback to its use is the unpleasant odor that it imparts to eructations. An enema of asafetida is one of the most reliable remedies that we possess in *tympanites* and *flatulent colic*.

Administration.—For continued use the drug is best administered in the form of pills or capsules. To children it may be conveniently administered in the form of suppositories. In tympanites the official emulsion (4–6 ounces–120.0–175.0 mls) should be employed as an enema.

VALERIANA

(Valerian)

Valerian is the dried rhizome and roots of *Valeriana officinalis*, a native of Europe. It contains a volatile oil, to which it owes most of its activity, and valeric acid and tannin.

PREPARATIONS	DOSES
Tinctura Valerianæ.....	$\frac{1}{2}$ –1 fl. dr (2.0–4.0 mils)
Tinctura Valerianæ Ammoniata (made by macerating valerian in aromatic spirit of ammonia) ..	20–30 min. (1.2–2.0 mils)

Therapeutics.—Valerian is often of service in subduing the various nervous phenomena occurring in persons of excitable temperament. It has been especially esteemed in *hysteria*. Whether its efficacy is due to a direct influence on cerebral control or to a psychic effect induced by its strong odor and flavor is not clear. It is also apparently of value at times in the treatment of *diabetes insipidus*.

Ammonii Valeras, U. S. P. (Ammonium Valerate), Zinci Valeras, U. S. P. (Zinc Valerate) and Ferri Valeras (Iron Valerate) are employed for the same purposes as valerian, but they are less effective. They are given in doses of from 1 to 5 grains (0.06–0.3 gm.). The following pill of the three valerates is frequently prescribed as a tonic and antispasmodic:

R. Ferri valeratis,
Zinci valeratis,
Quinina valeratis..... āā gr. xx (1.3 gm.).—M.
Fiant pilulæ No. xx.
Sig.—One after meals.

SPIRITUS ÆTHERIS COMPOSITUS

(Compound Spirit of Ether, Hoffmann's Anodyne)

Hoffmann's anodyne is a colorless, inflammable liquid, having an ethereal odor and taste. It consists of 325 parts by volume of ether, 650 parts of alcohol, and 25 parts of ethereal oil, the last being an ethereal solution of a product of the distillation of sulphuric acid and alcohol. The dose is from $\frac{1}{2}$ to 1 fluidram (2.0–4.0 mils).

Pharmacologic Action and Therapeutics.—Hare concludes from a careful study of this compound that its calmarative effects are largely due to the ether which it contains rather than to the ethereal oil, and that each of its ingredients stimulates the system—the ether the most, and the ethereal oil the least powerfully.

Hoffmann's anodyne is an excellent carminative for expelling gas from the stomach. It affords prompt relief in severe *paroxysmal palpitation* dependent upon gastric flatulence. It is often of service in *angina pectoris*, especially when the attacks are precipitated by flatulency. In *chronic valvular disease*, when compensation is partially lost and the patient suffers from restlessness, dyspnea, and insomnia, the compound spirit of

ether is often a useful adjuvant to other remedies. It is sometimes efficacious in *hiccough*. A combination such as the following will sometimes be found useful in *asthma*:

R̄. Ammonii bromidi..... ʒij (8.0 gm.)
 Tincturæ belladonnæ..... fʒj (4.0 mls)
 Tincturæ lobeliæ..... fʒij (8.0 mls)
 Spiritus ætheris compositi..... fʒss (15.0 mls)
 Elixiris aromatici..... q. s. ad fʒiij (90.0 mls).—M.
 Sig.—A dessertspoonful in water every two hours during the paroxysm.

The following mixture is serviceable in severe *gastric flatulency*:

R̄. Spiritus ætheris compositi
 Spiritus camphoræ..... āā ℥xv (1.0 mil)
 Spiritus menthæ piperitæ..... ℥v (0.3 mil).—M.
 Sig.—To be taken in water.

MOSCHUS, U. S. P.

(Musk)

Musk is the dried secretion from the preputial follicles of *Moschus moschiferus*, a species of deer found in Central Asia. It appears as reddish-black unctuous grains having a peculiar penetrating odor and a bitter aromatic taste. The dose is from 5 to 15 grains (0.3–1.0 gm.).

PREPARATION

DOSE

Tinctura Moschi, U. S. P. (5 per cent.).. ½–2 fl. dr. (2.0–8.0 mls)

Therapeutics.—Musk is used as an antispasmodic and as a general stimulant. As Graves first pointed out, it is a valuable stimulant in *typhoid fever* and *kindred affections*, when there are profound nervous exhaustion and circulatory failure. It is also of service in *obstinate hiccough*. Important drawbacks to its use are its costliness and the difficulty in obtaining an unadulterated preparation.

CIMICIFUGA, U. S. P.

(Black Snakeroot, *Actæa Racemosa*)

Cimicifuga is the dried rhizome and rootlets of *Cimicifuga racemosa*, a perennial plant growing in the woodlands of North America. It contains a resin, a bitter neutral substance, and a volatile oil.

PREPARATIONS

DOSE

Fluidextractum Cimicifugæ, U. S. P..... 10–30 min. (0.6–2.0 mls)
 Extractum Cimicifugæ, U. S. P..... 2–8 gr. (0.1–0.5 gm.)

Pharmacologic and Therapeutic Action.—In large doses *cimicifuga* causes nausea, headache, vertigo, tremors, muscular relaxation, slowing and weakening of the pulse, anesthesia, and, finally, paralysis of respiration. The anesthesia is due, according to Hutchinson, to paralysis of the sensory mechanism of the spinal cord. The weakness of the pulse is probably due to a direct depressant effect exerted on the heart itself.

Cimicifuga is apparently of little value. Good results have been claimed for it in *simple chorea* and *dysmenorrhea*. Ringer found it useful, in combination with *gelsemium*, in the *nervous disturbances attending the menopause*.

LACTUCARIUM, U. S. P.

(Wild Lettuce)

Lactucarium is the concrete milk-juice of *Lactuca virosa*, a biennial herb cultivated chiefly in Central and Southern Europe. The dose is from $\frac{1}{2}$ to 1 dram (2.0–4.0 gm.).

PREPARATIONS

DOSE

Tinctura Lactucarii, U. S. P.....	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls)
Syrupus Lactucarii, U. S. P.....	1–4 fl. dr. (4.0–15.0 mls)

Therapeutics.—*Lactucarium* is supposed to possess feeble somnifacient properties, but it is of little value. It was formerly used for *cough*, but it has been largely abandoned.

HUMULUS, U. S. P.

(Hops)

Hops are the dried strobiles of *Humulus Lupulus*, a perennial climber largely cultivated in Europe and the United States. They have an aromatic odor, and a bitter, slightly astringent taste. A glandular powder separated from the dried strobiles is known as *lupulin*. The latter appears in the form of minute yellowish-brown, resinous granules, having a bitter aromatic taste. The chief constituents of hops are a volatile oil, lupamaric acid (the bitter principle), and a resin. The dose of lupulin is from 5 to 15 grains (0.3–1.0 gm.).

PREPARATIONS

DOSE

Fluidextractum Lupulini.....	5–30 min. (0.3–2.0 mls)
Oleoresina Lupulini.....	2–5 gr. (0.13–0.3 gm.)

Therapeutics.—Hops act as a bitter tonic and as a feeble narcotic. They have been used with some success in failure of digestion due to *atony of the stomach* and in the *milder forms of insomnia*.

SUMBUL, U. S. P.

(Musk-root)

Sumbul is the root of *Ferula Sumbul*, a perennial herb growing in Central Asia. Its chief constituents are a resin, to which its musk-like odor is due, a fixed oil, and angelic acid. The dose of the root is from 10 to 30 grains (0.6–2.0 gm.).

PREPARATIONS

DOSE

Fluidextractum Sumbul, U. S. P.....	½–1 fl. dr. (2.0–4.0 mils)
Extractum Sumbul, U. S. P.....	2–5 gr. (0.1–0.3 gm.)

Therapeutics.—Sumbul is sometimes used as an antispasmodic in *hysteria* and allied neuroses. In *neurasthenia* the extract may be given in pill with iron and arsenic. The following combination, suggested by Bradbury, is often effective in relieving the insomnia, mental depression, and flashes of heat commonly occurring at the *menopause*:

℞. Sodii bromidi.....	℥iiss (10.0 gm.)
Fluidextracti sumbul	
Tincturæ humuli.....	āā f℥i (30.0 mils)
Spiritus camphoræ.....	f℥ij (8.0 mils)
Syrupi zingiberis.....	q. s. ad f℥iv (120.0 mils).—M.
Sig.—Two teaspoonfuls in water after meals.	

VIBURNUM PRUNIFOLIUM, U. S. P.

(Viburnum; Black Haw)

Officially viburnum prunifolium is the bark of a tall shrub of the same name, growing in the eastern and southern states of North America. It contains a resin (viburnin) and valeric acid.

PREPARATIONS

DOSE

Fluidextractum Viburni Prunifolii, U. S. P.....	½–1 fl. dr. (2.0–4.0 mils)
Extractum Viburni Prunifolii, U. S. P.....	5–10 gr. (0.3–0.6 gm.)

Therapeutics.—Large doses of viburnum are said to have a mild depressant action on the central nervous system, but the evidence is far from convincing. Good results have been claimed for the drug in *various menstrual disorders*, particularly *dysmenorrhea*, and in the *nervous disturbances attending the menopause*.

SPINAL CORD EXCITANTS

Spinal cord excitants, or excitomotors, are drugs that increase reflex excitability, their effect in toxic doses being sufficient to induce tetanic convulsions. They may act by directly stimula-

ting the motor cells of the spinal cord or by depressing the inhibitory function of the receptive neurons, thus giving sensory stimuli more ready access to the motor cells. The following drugs have an excitomotor action:

Strychnin	Hydrastin
Caffein	Calabarin (see p. 154)
Thebain (see p. 86).	

Strychnin and caffein are the only members of the group that sensibly increases reflex excitability in ordinary doses, and with caffein the stimulant effect on the spinal cord is overshadowed by that on the cerebrum and medullary centers. As an excitomotor, strychnin is useful in various conditions of depression of the central nervous system and in muscular atony due to depression or temporary loss of reflex excitability.

NUX VOMICA, U. S. P.

Nux vomica is the seeds of the *Strychnos Nux-vomica*, a small tree growing in the East Indies. It contains two alkaloids, *strychnin* and *brucin*. Strychnin fully represents the action of the crude drug. It is official as *Strychnina*, which is very sparingly soluble in water, as *Strychninæ Nitras*, which is soluble in 42 parts of water, and as *Strychninæ Sulphas*, which is soluble in 31 parts of water. All these preparations appear as colorless crystals or white crystalline powders, having an intensely bitter taste. Brucin resembles strychnin in its action, but is less powerful. The dose of strychnin or of either of its salts is from $\frac{1}{60}$ to $\frac{1}{20}$ grain (0.001–0.003 gm.).

PREPARATIONS	DOSE
Extractum Nucis Vomicae, U. S. P.	$\frac{1}{8}$ – $\frac{1}{4}$ gr. (0.008–0.016 gm.)
Fluidextractum Nucis Vomicae, U. S. P. . . .	1–3 min. (0.06–0.2 mil)
Tinctura Nucis Vomicae, U. S. P.	5–20 min. (0.3–1.2 mils)
Pulvis Nucis Vomicae.	$\frac{1}{2}$ –3 gr. (0.03–0.2 gm.)

Strychnin enters into the elixir of the phosphates of iron, quinin and strychnin (Elixir Ferri, Quininae et Strychninae Phosphatum) and the compound syrup of hypophosphites (Syrupus Hypophosphitum Compositus), but neither of these preparations is official.

Pharmacologic Action.—Strychnin, when taken by the mouth, produces a stomachic effect, owing to its intensely bitter taste. After absorption it increases the reflex excitability of the spinal cord and medullary centers.

Nervous System.—The dominant action of strychnin is on the spinal cord. In vertebrate animals even moderate doses intensify the irritability of the reflex mechanism, so that weaker

afferent stimuli are effective in producing the usual muscular responses, while toxic doses cause such extreme reflex excitability that the slightest sensory impulses result immediately in generalized tetanic convulsions. The convulsions are clearly of spinal origin, for they occur after the cord has been divided in the cervical region, and they do not occur in muscles that have been separated from the spinal cord by section of the supplying nerve, or in muscles that have had strychnin injected into them after their arterial connections with the general circulation have been cut off by ligature. Although it is evident that the convulsions of strychnin-poisoning are the result of an effect produced within the spinal cord, there is reason for believing that they are due not so much to direct stimulation of the motor cells in the anterior horns as to lessened resistance in the receptive or sensory neurons of the cord, whereby slight impulses from the periphery are capable of producing maximal reflex responses, and instead of reaching and influencing but a limited number of motor cells, as is normally the case, are permitted to spread out and excite the motor cells of the entire cord. Thus, in the frog, convulsions do not result from strychnin injections after the skin has been anesthetized by dipping the animal in a solution of cocain, nor do they occur after division of all the posterior nerve roots, unless a stimulus is applied to one of the central stumps of the roots. By increasing the sensitiveness of the central reflex mechanism, strychnin tends to improve the tone of the muscles throughout the body.

In the higher animals strychnin stimulates the reflexes of the medulla and cerebrum, as well as those of the spinal cord. In the medulla large doses tend to increase the sensitiveness of the respiratory, vasoconstrictor and cardio-inhibitory centers, the effect on respiration being especially pronounced when the respiratory center has been previously depressed by morphin or some other narcotic. In the cerebrum even ordinary doses increase the acuity of vision, hearing, taste and smell. Upon the psychic and motor functions the drug has a stimulating effect similar to that of caffein, but very much less pronounced.

After a time in poisoning the stimulating effects of strychnin are followed by those of paralysis, the medullary centers and the spinal cord both sharing in the depression. The paralytic effect first shows itself in the interval between the convulsions, but finally it becomes the dominant feature. It is due not merely to exhaustion of the nervous system by the repeated convulsions, but to the direct depressant action of the drug itself.

Circulatory System.—Moderate doses of strychnin have little effect on the circulation, although they may slightly raise the

blood pressure by stimulating the vasoconstrictor center and slightly slow the pulse by stimulating the cardio-inhibitory center. During the convulsive stage of poisoning by the drug, however, there is a marked rise of blood pressure, this effect being due partly to direct stimulation of the vasoconstrictor center, partly to the violent muscular contractions and partly to the asphyxia. Ordinary doses of the drug have no direct effect on the heart itself, but large toxic doses depress it.

Respiration.—By increasing the sensitiveness of the respiratory center, strychnin tends to strengthen the respiratory movements, this effect being more marked when the center has previously been depressed. In poisoning the center is first stimulated and then depressed.

Muscles.—While strychnin probably has no direct effect on the muscles, ordinary doses increase their tone and functional capacity by increasing the excitability of the spinal reflexes.

Alimentary Canal.—Taken by the mouth, strychnin and the various preparations of *nux vomica*, like other very bitter substances, whet the appetite and probably increase the secretion of gastric juice, when owing to some functional disturbance this is deficient. Through its action on the spinal centers, it is likely that the drug improves the tone of the gastric and intestinal muscles, and by increasing the sensitiveness of the defecation reflex, it enhances the effect of laxative remedies.

Metabolism.—Large doses of strychnin by stimulating muscular activity increase metabolism, as shown by the greater intake of oxygen and greater output of carbon dioxide.

Absorption and Elimination.—Strychnin is absorbed rapidly, chiefly from the intestines. A part of the drug is destroyed in the tissues, and the remainder is excreted unchanged, mainly in the urine. While excretion is virtually completed within 36 or 48 hours, traces of the alkaloid may be found for 5 or 6 days. Whether any degree of tolerance for strychnin can be acquired by continuous administration is a debatable question, but clinical experience suggests an affirmative answer.

Toxicology.—The first evidences of the toxic effect of strychnin are restlessness, twitching of the muscles, and a feeling of anxiety. If the dose has been sufficiently large, general tetanic convulsions speedily develop, the body assuming the position of *orthotonos* or *opisthotonos*. The convulsions last from a few seconds to a minute, and recur in response to any slight stimulus, such as a touch, a noise, or even the movement of a limb. In the intervals there is complete muscular relaxation with marked physical depression. In fatal cases the convulsions become more severe and recur at decreasing intervals, and finally death

ensues from exhaustion and paralytic asphyxia or during a convulsion from spasmodic fixation of the respiratory muscles. Throughout the attack the stomach is usually retentive and the mind remains clear, although toward the end there may be coma, as the result of asphyxia. The average fatal dose of strychnin for man is from $1\frac{1}{2}$ to 2 grains (0.1–0.13 gm.).

The history of the case, the presence of a wound, the gradual onset, the early involvement of the muscles of the jaw (trismus), the persistent muscular rigidity and the protracted course will serve to distinguish *tetanus* from strychnin-poisoning. The history of the case, the varying attitudes, the wide range of the convulsive movements, and the facial display of emotion will serve to distinguish *hysteria* from strychnin-poisoning.

Treatment.—If symptoms have already appeared no attempt should be made to wash out the stomach until the exaggerated reflex excitability has been subdued by inhalations of chloroform. Tannin, 10 grains (0.65 gm.), or potassium permanganate, 3 grains (0.2 gm.) in a glass of water, may be administered at short intervals as a chemical antidote. After the use of tannin, lavage must be practised, otherwise the tannate of strychnin precipitated in the stomach will be slowly absorbed. The best physiologic antidotes are ether by inhalation, chloral (30 gr.—2.0 gm.), bromids in large doses, and paraldehyd. The chloral and bromid may be given by the rectum. Other useful measures are artificial respiration, the application of external heat, inhalations of oxygen, and intravenous infusion of normal saline solution.

Therapeutics.—Nux vomica, or its chief alkaloid strychnin, is used chiefly as a circulatory stimulant, a respiratory stimulant, an excitomotor, a general tonic, and a stomachic.

As a Circulatory Stimulant.—Although strychnin has very little direct effect on the circulation, it is often of service in cardiac weakness from various causes, its good effects being due probably to its capacity for intensifying the reflex activity of the spinal cord and medulla, thus increasing the muscular tone throughout the body and improving the general nutrition. In *valvular disease of the heart with decompensation* it often renders good service as an adjuvant to digitalis, but it is of little value when used alone. In acute infections, notably *pneumonia*, *typhoid fever*, *influenza* and *diphtheria*, it is especially useful in tiding over periods of pronounced circulatory depression. In *chronic myocardial degeneration* it is also efficacious. It is often given in *surgical shock*, although many surgeons of large experience believe that it is of no value.

As a Respiratory Stimulant.—Strychnin is a useful respiratory stimulant in depression of the respiratory center from

narcotic poisoning, as by *morphin*, *chloral*, *chloroform*, *ether*, etc., and from diseases of the respiratory tract, such as *pneumonia*, *chronic bronchitis*, *pulmonary emphysema* and *advanced pulmonary tuberculosis*. In *pulmonary emphysema* no single drug is so useful.

As an Excitomotor.—When paralysis is the result of complete destruction of nerve-cells or fibers, strychnin, like all other drugs, will be ineffective; but when the loss of power is the result simply of depression or exhaustion of the nervous mechanism, it may prove useful. It is often prescribed in the *hemiplegia* following apoplexy, but it is valueless in this condition, except, perhaps, as a general tonic. On the other hand, in the various forms of *peripheral neuritis*, such as *plumbic*, *alcoholic*, *diphtheritic*, and that due to pressure, it is sometimes of considerable service. It should not be used, however, until all acute symptoms of the affection have subsided.

In *neurasthenia* minute doses of strychnin with arsenic are sometimes efficacious, but more often the drug is useless or actually harmful. In *amaurosis* from tobacco, alcohol, or lead it is frequently of value.

It is thought that intramuscular injections of strychnin aid in restoring power to the affected muscles in *acute poliomyelitis*. This treatment, however, should not be instituted until several weeks after the incidence of the disease. *Nux vomica* often affords relief in *incontinence of urine* from atony of the bladder—a condition not rarely met with in old persons. It is contraindicated, of course, in enuresis due to increased irritability of the vesical sphincter. It is an excellent adjuvant to vegetable cathartics in *constipation* dependent upon atony of the bowel. It is a trustworthy remedy in the *marked flatulence* not uncommonly seen in elderly persons, as the result of atony of the gastrointestinal musculature. It is also of service in *atonic dilatation of the stomach* and in *postoperative paresis of the stomach and bowel*.

As a General Tonic.—Owing to its favorable effect upon the appetite, digestion, muscular activity and circulation, strychnin or *nux vomica* may often be used with advantage in *convalescence from exhausting illnesses*. Combined with iron and arsenic it is frequently beneficial in anemia from various causes.

As a Stomachic.—*Nux vomica* may often be advantageously substituted for the simple bitters, such as gentian and quassia, in *anorexia* due to chronic gastric diseases or following the acute infections. From 5 to 15 drops of the tincture, with or without hydrochloric acid, may be used with benefit in *indigestion* resulting from *atony of the stomach* or *mild gastric catarrh*. In

these cases the chief symptoms are a coated flabby tongue, poor appetite, a sense of fulness and discomfort (without actual pain) for some time after meals, flatulence, retarded evacuation of the stomach, and, in many cases, a deficient secretion of hydrochloric acid. Nux vomica and its alkaloids are contraindicated in gastric disorders with hyperchlorhydria or evidences of active inflammation.

Other Uses.—Dana, Dercum and others have found strychnin in very large doses of service in *trigeminal neuralgia* (*tic douloureux*), occurring in anemic and exhausted patients, and when the duration of the disease has not been more than one or two years. The drug is given hypodermically once a day, and the dose is gradually increased from $\frac{1}{30}$ of a grain to $\frac{1}{5}$ of a grain (0.002 to 0.013 gm.), from ten to twenty days being required to reach this maximum. Dana also reports good results in *myasthenia gravis* from the use of strychnin hypodermically in doses cautiously increased to $\frac{1}{4}$ grain (0.016 gm.), once or twice a day. A number of observers (Posner, Feilchenfeld, Ketly, Spaether) speak favorably of the action of strychnin in *diabetes insipidus*.

Administration.—Strychnin sulphate and extract of nux vomica are suitable preparations for use in pills. When a liquid preparation is desired, as in atony or dilatation of the stomach, the tincture will be found reliable. The nitrate of strychnin is sometimes preferred to the sulphate for hypodermic use, but it has no advantage over the latter. Nervous excitement, restlessness, and twitching of the muscles are indications that the limit of tolerance has been reached.

Incompatibles.—Strychnin is incompatible with tannin, alkalis, chlorids, iodids, and bromids.

SPINAL CORD DEPRESSANTS

Spinal cord depressants are drugs that decrease spinal reflex excitability. They may act on the motor neurons, impairing their capacity to discharge impulses, or they may act on the sensory neurons and thus protect the motor neurons from the influence of peripheral stimuli. Their action is opposed to that of strychnin. The following are the most important members of the group:

Ether
Bromids

Chloroform
Hydrated chloral.

The action of these drugs on the spinal cord is not selective, but secondary to that on the cerebrum.

Soluble magnesium salts, such as the sulphate, when injected intramuscularly, intravenously or intraspinally, powerfully depress both the sensory and motor mechanism of the entire central nervous system.

Spinal cord depressants are useful in controlling convulsions of spinal origin, such as occur in tetanus and strychnin-poisoning. Even in convulsions of cerebral origin they are not without value, for by depressing the lower motor neurons they impair their capacity to transmit impulses from the cerebrum to the muscles, and by depressing the lower sensory neurons they afford the cerebrum more or less protection from the effects of external stimuli. The two less powerful members of the group, bromids and chloral, especially the bromids, are also of service in allaying minor grades of nervous hyperexcitability, such as are seen in hysteria, hyperthyroidism, chorea, whooping cough, laryngismus stridulus, persistent hiccough, hyperemesis (reflex), chordee, etc.

MOTOR NERVE STIMULANTS

The only stimulant of the motor nerve-endings that merits consideration is *physostigmin*, and even this drug has much more important actions on the parasympathetic nerve-endings in the smooth muscle of the eye (miosis) and intestine (strengthening contractions). Guanidin, a constituent of creatin, has a similar action on motor nerves, but it is not used for medicinal purposes. Nicotin first stimulates and then depresses the nerve-endings in the skeletal muscles experimentally. These substances produce fibrillary muscular contractions, which persist after section of the motor nerve, but which are suppressed by curare and magnesium. There are no clinical indications for using physostigmin as a stimulant of the motor nerve-endings in voluntary muscles.

PHYSOSTIGMA, U. S. P.

(Calabar Bean)

Physostigma is the seed of *Physostigma venenosum*, a perennial climber, growing in West Africa. It contains two alkaloids, *physostigmin* or *eserin*, and *calabarin*; the latter is much less important than the former and resembles strychnin in its action.

PREPARATIONS

DOSE

Tinctura Physostigmatis, U. S. P. . . . 5-30 min. (0.3-2.0 mils)
 Extractum Physostigmatis, U. S. P. $\frac{1}{8}$ - $\frac{1}{4}$ gr. (0.008-0.015 gm.).

Physostigmin, or eserine, fairly represents the active properties of the bean. It is official in the form of physostigmin salicylate

(*Physostigminæ Salicylas*), which occurs in colorless or faintly yellow crystals, soluble in 75 parts of water or 16 of alcohol. The dose is from $\frac{1}{100}$ to $\frac{1}{40}$ grain (0.00065–0.0015 gm.).

Pharmacologic Action.—Circulatory System.—Small therapeutic doses of physostigmin do not affect the circulation. Large doses tend to decrease the pulse-rate and to raise slightly the blood pressure. The first of these effects is probably due to peripheral vagus stimulation, and the second to stimulation of the vasoconstrictor nerves and contraction of the arterioles. Toxic doses lower the blood pressure by depressing the vasoconstrictor center and the heart itself.

Nervous System.—The dominant action of physostigmin is on the peripheral nerves. It has a pronounced stimulating effect on the parasympathetic nerve-endings in unstriated muscle, especially that of the eye and intestine, although it tends to contract also that of the bladder, ureters, bronchi and arterioles. Strong concentrations also stimulate the motor nerve-endings in striped muscle, causing fibrillary twitchings. Like pilocarpin, physostigmin stimulates the nerve-endings in the secretory glands, but its effect on the secretions is largely inhibited by peripheral vasoconstriction and, in consequence, a reduced blood supply. The drug is mutually antagonistic to atropin in its actions on unstriated muscle and the secretory glands and with curare in its action on striped muscle.

The actions of physostigmin on the central nervous system are of secondary importance. It depresses somewhat the reflex excitability of the spinal cord and first stimulates and then depresses the medullary centers. The drug has little effect on the cerebrum and none on the sensory nerves.

Respiration.—Full therapeutic doses slightly increase the rate and depth of the respirations through a central stimulation. Toxic doses paralyze the respiratory mechanism and in fatal poisoning death is caused by asphyxia.

Alimentary Canal.—Physostigmin greatly increases the motor activity of the stomach and intestine and in toxic doses causes tonic contractions. These effects are due to stimulation of the parasympathetic (autonomic) nerve-endings.

Eye.—The instillation of a drop or two of a 1 per cent. solution of physostigmin salicylate into the eye is followed in a few minutes by miosis and spasm of accommodation, or near vision. The miosis reaches its maximum in about 30 minutes and then very gradually passes off, disappearing completely in 3 or 4 days. The spasm of accommodation begins somewhat later than the miosis and disappears more quickly. In addition to these effects applications of physostigmin cause a decrease in the

intraocular tension and not rarely painful twitching of the eyelid. The miosis is due to stimulation of the oculomotor endings in the sphincter muscle of the iris. That it is not due to paralysis of the sympathetic (dilator) mechanism is shown by the fact that stimulation of the cervical sympathetic still causes dilatation of the pupil after the use of physostigmin, and that it is not due to direct stimulation of the muscle substance is shown by the fact that no miosis occurs with physostigmin after the oculomotor endings have degenerated as a result of division of the post-ganglionic fibers of the oculomotor nerve, even though the muscle of the iris is still intact. The spasm of accommodation is caused by stimulation of the oculomotor endings in the ciliary muscle, and the lowering of the intraocular tension is brought about mainly by the miosis, which facilitates the escape of fluid from the anterior chamber of the eye by widening the spaces of Fontana, although it may be due in part also to decreased secretion—an effect of vasoconstriction.

Toxicology.—Physostigmin-poisoning is characterized by extreme muscular relaxation, tremors and twitchings of the muscles, abdominal cramps with vomiting and diarrhea, miosis, sweating, salivation, collapse and asphyxia. The *treatment* consists in evacuating the stomach, in administering tannin as a chemical, and atropin as a physiologic, antidote, and in combating circulatory and respiratory failure with stimulants.

Therapeutics.—Physostigma has a very limited range of usefulness. It is employed chiefly as a miotic and stimulant of the gastric and intestinal muscles.

As a Miotic.—Physostigmin salicylate is used to overcome the *mydriasis* produced by atropin, to lessen intraocular tension in the early stages of *acute glaucoma*, and sometimes alternately with atropin to break up fresh adhesions in *iritis*. In *peripheral ulceration of the cornea*, in the absence of *iritis*, it may sometimes be more efficacious than atropin.

In *glaucoma* physostigmin should be used in the strength of from 1 to 4 grains (0.065–0.26 gm.) to the ounce (30.0 mls), a drop or two of the solution being instilled about every two hours until relief is obtained.

As a Stimulant to the Gastric and Intestinal Muscles.—The extract of physostigma sometimes makes a useful addition to cathartic pills intended to relieve *atonic constipation*. Hypodermic injections of physostigmin salicylate— $\frac{1}{40}$ of a grain (0.0016 gm.)—alone, or with pituitary extract and strychnin, are of service in *postoperative intestinal paresis*, *acute dilatation of the stomach*, and *excessive tympanites* of typhoid fever and other infections.

Untoward Effects.—Strong solutions of physostigmin (0.5–1.0 per cent.), when instilled into the eye, frequently cause painful contractions of the eyelid and facial muscles. On standing, solutions of the alkaloid turn red, lose some of their effectiveness, and become more irritant.

MOTOR NERVE DEPRESSANTS

The following drugs, most of which are unimportant from a therapeutic viewpoint, have a depressant action on the peripheral ends of the motor nerves:

Curare	Gelsemium
Lobelia	Sparteïn
Conium	Nicotin
Magnesium salts	Muscarin.

CURARE

Curare is a resinous extract obtained from various species of *Strychnos*, growing in South America. Taken by the mouth, it has little or no effect, as it is poorly absorbed and rapidly destroyed, but when introduced into the body through an open wound or by subcutaneous or intravenous injection it is a powerful paralyzant of the end-plates of the motor nerves in all striated muscle, except that of the heart. Death results from paralysis of the muscles of respiration. Because of its highly selective action on the motor nerves, curare is extensively employed in physiologic and pharmacologic experimental work, but owing to its extremely poisonous properties and the uncertain dosage it has no therapeutic use.

LOBELIA, U. S. P.

(Indian Tobacco)

Lobelia is the dried leaves and flowing tops of *Lobelia inflata*, a weed growing in the wild places of Canada and the United States. Its chief constituent is the liquid alkaloid, *lobelin*. The latter forms crystalline salts, which are soluble in water.

PREPARATIONS	DOSE
Tinctura Lobeliæ, U. S. P.	10–30 min. (0.6–2.0 mils)
Fluidextractum Lobeliæ, U. S. P. .	2–5 min. (0.1–0.3 mil).

Pharmacologic Action.—Like nicotin, lobelia first stimulates and then depresses both the sympathetic and parasymp-

pathetic ganglia of the autonomic nervous system, stimulates and then depresses the central nervous system, and depresses the nerve-endings in muscle. By depressing the vagus endings it relaxes the bronchioles. Large doses cause vomiting, probably by stimulating the vomiting center in the medulla.

Therapeutics.—Lobelia was formerly employed as an emetic, but this use of the drug is now obsolete. Because of its power to relax the bronchioles, and, through its nauseating properties, to lessen the viscosity of the bronchial secretion, it is sometimes useful in *ordinary asthma with bronchial catarrh*. It is contra-indicated in so-called cardiac and renal asthma. To secure the best results it is necessary to give the drug in increasing doses until slight nausea is produced.

CONIUM

(Water Hemlock)

Conium is the full-grown fruit of *Conium maculatum*, gathered while still green. It contains a volatile oil and a yellowish, liquid alkaloid, *coniin*, which represents the active properties of the drug. Coniin forms with acids crystallizable salts. The dose of coniin hydrobromid, is from $\frac{1}{20}$ to $\frac{1}{6}$ grain (0.003–0.01 gm.).

PREPARATIONS

DOSE

Fluidextractum Conii.....	1–3 min. (0.06–0.2 mil)
Tinctura Conii.....	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls).

Pharmacologic Action.—The action of conium resembles that of nicotine, but it is somewhat more depressant to the end-plates of the motor nerves and to the central nervous system, and somewhat less depressant to the sympathetic and parasympathetic ganglia. Toxic doses produce a staggering gait, muscular relaxation, tremors, vertigo, ptosis and dilatation of the pupils, collapse and asphyxia. Consciousness and sensibility are retained until near the end of life.

Therapeutics.—Conium has been used as an antispasmodic in *chorea*, *paralysis agitans*, *asthma*, and *whooping cough*, but in these affections it is of less value than other remedies. In the form of vapor it is sometimes useful in allaying the cough of *bronchitis*. Spitzka and others strongly recommend it in the mental and physical excitement of *acute mania*. On account of the uncertain strength of the preparations, it is necessary to give the drug in small doses and to rapidly increase them until an effect is produced.

GELSEMIUM, U. S. P.

(Yellow Jasmine Root)

Gelsemium is the rhizome and root of *Gelsemium semper-virens*, a climber indigenous to the southern United States. It contains *gelseminin* and *gelsemin*. Gelseminin, which represents to a considerable extent the active properties of the crude drug, occurs in the form of white crystals, with a bitterish taste, sparingly soluble in water, and readily soluble in alcohol, ether, or dilute acids. The dose of gelseminin or its salts is from $\frac{1}{120}$ to $\frac{1}{50}$ grain (0.0005–0.0013 gm.).

PREPARATIONS

DOSE

Tinctura Gelsemii, U. S. P.....	5–15 min. (0.3–1.0 mil)
Fluidextractum Gelsemii, U. S. P..	2–5 min. (0.1–0.3 mil)
Extractum Gelsemii, U. S. P.....	$\frac{1}{8}$ – $\frac{1}{4}$ gr. (0.008–0.015 gm.).

Pharmacologic Action.—Gelsemium has an action similar to that of nicotin and coniin, but it is somewhat more depressant to the central nervous system. Toxic doses kill by paralyzing the respiratory center. Locally applied, gelseminin dilates the pupil of the eye and paralyzes accommodation, these effects being produced, as with atropin, by depression of the endings of the oculomotor nerve.

Gelsemium-poisoning is characterized by vertigo, headache, disordered vision, ptosis, extreme muscular weakness, collapse and asphyxia.

Therapeutics.—Gelsemium has been employed as an antispasmodic in *laryngismus stridulus*, *whooping cough*, *asthma*, and *chorea*, but in these affections there are much more efficient remedies. At one time gelseminin was recommended as a mydriatic, but homatropin and atropin are much superior. The drug is sometimes useful in *spasmodic affections of the muscles*, such as *torticollis*, and in *obstinate neuralgia*, especially of the trifacial nerve. In the latter, a combination of butyl-chloral hydrate (5 gr.–0.3 gm.) and gelseminin ($\frac{1}{100}$ gr.–0.0006 gm.), as recommended by Murrell, is said to be efficacious. Ringer found it useful in some cases of *Ménière's disease*. On account of the variability of the preparations, they should be given in small doses, gradually increased until such symptoms as vertigo or dimness of vision appear.

SPARTEINÆ SULPHAS, U. S. P.

Sparteïn is a liquid alkaloid from the tops of *Cytisus Scoparius*, or common broom. It is official as *Sparteïnæ Sulphas*, a white crystalline or granular powder of a somewhat bitter taste, and

freely soluble in water or alcohol. The dose of spartein sulphate is $\frac{1}{4}$ grain (0.015 gm.), cautiously increased to 1 grain (0.06 gm.).

Pharmacologic Action.—Sparteín closely resembles coniín in its actions, although it is less depressant to the central nervous system and is less poisonous. The drug also depresses the heart directly and so decreases both the force and frequency of the cardiac contractions. It has been employed somewhat extensively as a substitute for digitalis in cardiac insufficiency, but the actions of the two drugs are entirely dissimilar.

NICOTIN

Nicotin, the active principle of tobacco (*Nicotiana Tabacum*), is a volatile liquid alkaloid with intensely poisonous properties. The dried leaves of tobacco also contain traces of other alkaloids and a volatile oil. The smoke, in addition to nicotin, contains pyridin and other pyrogenous compounds, carbon monoxid, traces of hydrocyanic acid, phenols, and aldehyds.

Pharmacologic Action.—Nicotin first stimulates and then powerfully depresses both the sympathetic and the parasympathetic ganglia of the autonomic nervous system; it also stimulates and then depresses the central nervous system and the endings of the motor nerves in voluntary muscles. When injected directly into the circulation the drug first causes a transient elevation of blood pressure and slowing of the pulse. These effects are due to stimulation of the vasomotor center and the vagus center and ganglia. With large doses the secondary effects on the circulation are a fall of blood pressure and marked quickening of the pulse. These effects are due to depression of the peripheral vasomotor and cardio-inhibitory mechanisms. Nicotin first stimulates and then depresses the respiratory center. Large doses produce nausea and vomiting, partly through peripheral action, but chiefly through stimulation of the medulla.

Acute tobacco poisoning is due mainly to the effects of nicotin, although pyridin and other toxic constituents may have some influence. It is characterized by pallor, dizziness, faintness, sweating, palpitation, muscular weakness and collapse. **Chronic tobacco poisoning**, the result of excessive smoking, may produce the following symptoms: Cough, from irritation of the respiratory tract; various digestive disturbances, probably also due to the irritant action of the nicotin; palpitation and irregular action of the heart; headache, insomnia, irritability, tremors, and ready mental and physical fatigue; and occasionally dimness of vision (tobacco amblyopia), the result of retrobulbar optic neuritis. It is characteristic of chronic tobacco poisoning, except in very severe cases, that the symptoms soon subside on the discontinu-

ance of the drug. Evidence based on experiment that excessive smoking can produce organic changes in the vessels and heart is not convincing, although the results of certain recent investigations point in this direction. It is generally admitted, however, that excessive smoking is quite capable of provoking anginal attacks in persons who already have organic cardiovascular disease, and that the precordial pains sometimes disappear promptly after the complete withdrawal of the drug. It is possible, too, that the immoderate use of tobacco may sometimes cause such extreme irritability of the nerve centers that slight perturbations reaching them from the heart may result in anginal pain, even in the absence of any organic changes in the heart or vessels. Tobacco is unimportant from the viewpoint of practical therapeutics.

SENSORY NERVE DEPRESSANTS

When applied locally a drug may lessen or abolish sensation through an elective depressant action on the sensory nerves or, as is the case with ethyl chlorid and ether in the form of a fine spray, through the intense cold produced by its evaporation. A few drugs when given internally, if the dose is sufficiently large, produce a slight anesthetic effect through a peripheral action. This is true of *aconite* and the *bromids*.

Sensory nerve depressants are employed locally to relieve pain and allay itching. The following drugs act as local anesthetics:

Cocain		Quinin and urea hydrochlorid
Tropacocain		Magnesium sulphate
Betaeucain (Eucaïn)		Chlorbutanol (chloretone)
Procain (Novocain)		Dionin
Stovain	Esters of ben- zoic acid	Phenol
Alypin		Aconite
Benzyl alcohol		Veratrin
Orthoform		Hydrocyanic acid
Benzocain (Anesthesin)		Ethyl chlorid
Phenacain (Holocain)		Ether
Apothesine		
Saligenin		

Many of the *essential oils*, such as oil of mint and oil of cloves, also possess local analgesic properties.

Of the esters of benzoic acid, orthoform and benzocain (anesthesin), being but slightly soluble, are unsuitable for injection. Their anesthetic power is somewhat weaker but more persistent than that of the more soluble compounds. They are especially useful for painful ulcerations of the skin or mucous membranes.

Of the soluble synthetic anesthetics, betaeucain, benzyl alcohol, alypin, and phenacain (holocain) are especially suitable for application to mucous membranes. Phenacain is used chiefly in the eye and alypin in the urethra.

Procaïn (novocain), betaeucain, apothesine and saligenin are especially effective for injection anesthesia. These are all safer than cocain, but betaeucain is much more irritant. Of the non-synthetic anesthetics, quinin and urea hydrochlorid produces a much more persistent anesthesia than any of the other soluble compounds, but is more irritant.

Tropacocain and stovain are less toxic than cocain, but somewhat more irritant. They are used especially for spinal anesthesia.

Chlorbutanol, dionin, phenol, aconite, veratrin, and hydrocyanic acid are relatively feeble anesthetics. Dionin (ethyl morphin) is used chiefly in inflammatory conditions of the eye, especially keratitis. It combines the action of an analgesic with that of a lymphagogue. Phenol and hydrocyanic acid are employed especially in pruritus.

Ethyl chlorid and ether produce local anesthesia through refrigeration; their effect is, therefore, transitory. They are useful in minor operations requiring but a single incision or puncture.

COCAINA, U. S. P.

(Cocain)

Cocain is an alkaloid obtained from the leaves of *Erythroxylon Coca*, a shrub indigenous to Peru and other South American States. Chemically, it is the methyl-benzoyl ester of ecgonin, which is closely related to tropin the basic constituent of atropin. Prolonged boiling decomposes cocain into methyl alcohol and benzoyl-ecgonin.

Both cocain itself and its hydrochlorid are official. The dose of either the free alkaloid or its salt is from $\frac{1}{8}$ to $\frac{1}{2}$ grain (0.008–0.03 gm.).

Pharmacologic Action.—Local Action.—Cocain is a general protoplasmic poison, which electively affects the sensory nerves, dilute solutions temporarily abolishing sensation without materially depressing other structures. More concentrated solutions also depress the motor nerves, but without producing in them any structural changes. Very strong solutions exert a paralyzing effect on all tissue cells and may even damage them permanently. There are four different methods of producing local anesthesia with solutions of cocain: (1) surface application; (2) injection into and beneath the skin (infiltration anesthesia);

(3) injection around or into nerve trunks (nerve blocking—regional anesthesia); (4) injection into the spinal canal around the posterior nerve roots (subdural or spinal anesthesia).

The direct application of a cocain solution to a mucous membrane or raw surface is followed in a few minutes by insensitiveness, which lasts from 15 to 30 minutes, according to the concentration employed. The various sensations, however, are not equally affected. Pain sense is promptly suppressed, but the sensations of touch and temperature yield less rapidly and less completely. In addition to local anesthesia, applications of cocain also produce marked vasoconstriction, which results in blanching and shrinking of the tissues and diminished secretion. This vasoconstricting action is useful in delaying the absorption of the drug, and thereby intensifying and prolonging its local effect. Moreover, in case of operation it tends to keep the part free of blood. So important is the rôle played by vasoconstriction in the production and maintenance of local anesthesia and in lessening the danger of poisoning from the rapid absorption of the drug, that it is advisable to restrict the local circulation still further by the addition of epinephrin to the cocain solution. Inflammation, owing to the accompanying hyperemia, impairs the anesthetizing effect of cocain.

Applications of cocain to the intact skin are without effect, as the horny layer of the epidermis is impermeable to the drug.

Eye.—The instillation into the eye of a few drops of a 4 per cent. solution of cocain hydrochlorid, after causing momentary irritation, results in anesthesia of the cornea and conjunctiva, local anemia, dilatation of the pupil, abolition of the winking reflex, slight retraction of the eyelids, and sometimes slight exophthalmos. The mydriasis, which lasts but a few hours, is not maximal, and is not accompanied by loss of reaction to light, paralysis of accommodation, or increase in the intraocular tension. It is largely of peripheral origin, for it can be produced in an excised eye. That it is due to stimulation of the sympathetic nerve-supply of the radial muscles of the iris, and not to paralysis of the oculomotor nerve-endings in the sphincter of the iris, as occurs with atropin, is shown by the fact that cocain no longer dilates the pupil after extirpation of the superior cervical ganglion, provided its application to the eye is delayed until degeneration of the sympathetic nerve-endings has occurred as a result of the operation. Although mydriatics as a class increase the intraocular tension by narrowing the spaces of Fontana and the canal of Schlemm, thus impeding the escape of the aqueous humor, cocain is without this action, probably because its vasoconstricting effect results in a compensatory reduction of

secretion. Accommodation remains nearly normal after the use of cocain, because the drug has no action on the ciliary muscle. Strong solutions of cocain have a destructive effect on the corneal epithelium and may produce permanent opacities.

Central Nervous System.—Cocain first stimulates and then depresses the central nervous system—cerebrum, medulla, and spinal cord. Both the psychic and motor areas of the cerebrum are affected, large doses first inducing wakefulness, mental exhilaration, physical unrest, and then more or less depression. Toxic doses not rarely cause clonic convulsions of cerebral origin. The injection of a small quantity into the spinal canal, by acting directly on the posterior nerve-roots, causes complete anesthesia of the entire lower half of the body, without any disturbance of consciousness. No depression of the sensory nerve-endings, however, is observed after the internal administration of the drug, even in toxic doses.

Circulatory System.—Moderate doses of cocain increase the pulse-rate and raise the blood pressure. The quickening of the pulse is due to stimulation of the accelerators and probably in part also to depression of the vagus center. The rise in blood-pressure is due chiefly to stimulation of the vasoconstrictor center, for it is not observed after section of the spinal cord. There is probably no direct effect on the arteries, such as results from the local application of the drug. Toxic doses of cocain lower the blood pressure and cause collapse by depressing both the vasoconstrictor center in the medulla and the heart itself.

Respiration.—In moderate doses cocain increases both the rate and depth of the respirations by stimulating the respiratory center. Toxic doses make the respiratory movements shallow and irregular, and finally cause death by asphyxia.

Muscles.—Although cocain has no direct effect on the muscles, it increases the capacity for muscular work and lessens the sense of fatigue by stimulating the motor and psychic areas in the cerebrum.

Temperature.—Toxic doses often cause a marked rise in temperature. The mechanism of this pyrogenic action is not definitely known, but it is not improbable that it is due to increased excitability of the heat-regulating centers.

Absorption and Elimination.—In solutions too dilute to cause vasoconstriction, cocain is rapidly absorbed both from the alimentary tract and the subcutaneous tissues. Much of the drug is destroyed in the body, but a part is excreted unchanged in the urine.

Toxicology.—The symptoms of **acute poisoning** vary with the rapidity of absorption. With somewhat slow absorption of a

toxic dose the usual symptoms are restlessness and excitement, then delirium, hurried respiration, acceleration of the pulse, mydriasis, increased body-temperature, vomiting, and finally, convulsions, unconsciousness, Cheyne-Stokes breathing, collapse and asphyxia. With rapid absorption, such as may occur after subcutaneous injections, there may be sudden syncope, with or without convulsions, and death within a short period, even a few minutes.

The *treatment* is purely symptomatic. When there are symptoms of respiratory and circulatory failure, such drugs as ammonia, caffeine and atropin are indicated. Artificial respiration should also be instituted. When excitement and convulsions are the conspicuous features, bromids may be given by the mouth and ether by inhalation, although it must not be forgotten that the use of these narcotics may increase somewhat the danger from respiratory depression.

Untoward Effects of Medicinal Doses.—There is a very wide variation in individual susceptibility to cocaine. Occasionally the local application of the drug to the nose or throat, even in solutions of moderate strength, is followed by intense excitement, syncope, or collapse.

Chronic Poisoning (Cocainism).—A potent cause of the cocaine-habit has been the frequent use of the drug in diseases of the nose and throat. Tyson states that he has known three successive chiefs of clinic in nose and throat dispensary service to acquire the habit. The habit is also common among those addicted to other narcotics, such as opium, alcohol, and chloral. The drug may be taken by the mouth, injected subcutaneously, or used as a snuff. The chief symptoms are emotional excitement, physical unrest, mental impairment, moral turpitude, hallucinations, mild epileptiform attacks, dilatation of the pupils, a rapid, feeble pulse, severe gastric disturbance, wasting, and anemia. When cocaineism is uncomplicated the prognosis is guardedly favorable. The drug should be withdrawn rapidly but not suddenly. Treatment in a sanatorium is always advisable. Scopolamin, atropin and strychnin are favorite substitutes. Hygienic and dietetic measures intended to improve general nutrition are indicated.

Therapeutics.—Cocaine is employed as a local anesthetic, simple mydriatic, and rarely as a respiratory stimulant.

Local Anesthetic.—As a local anesthetic cocaine has a very wide range of usefulness. In the various operations on the eye, nose, throat, urethra, and rectum it is indispensable. If possible, the mucous membrane should be washed with salt solution and then dried before the anesthetic is applied. In minor surgical

operations, such as amputation of the fingers, removal of small neoplasms, opening of small abscesses, it may also be employed with advantage. In these cases care must be taken to prevent undue absorption of the drug, and this is best accomplished by the application of a tight rubber band to the proximal side of the part to be operated on, thus controlling the circulation. A 2 per cent. solution may be injected to the extent of a dram (4.0 mls) with safety. The capillary oozing should not be checked immediately, as it serves to carry off the cocain. The same quantity of cocain in weak solution is distinctly less toxic than it is when in strong solution (Custer).

In operations in which the circulation cannot be controlled, and in which much of the solution must be allowed to remain in the tissues, the method employed by Schleich, known as *infiltration anesthesia*, is of great value. Schleich employs solutions of three strengths. The one of medium strength consisting of—

R. Cocain hydrochlorid.....	1 gr. (0.065 gm.)
Morphin hydrochlorid.....	½ gr. (0.03 gm.)
Sodium chlorid.....	2 gr. (0.13 gm.)
Sterilized distilled water.....	2 fl. oz. (60.0 mls)

The stronger solution contains 2 gr. (0.13 gm.) of cocain, and the weaker solution, $\frac{1}{10}$ grain (0.0065 gm.).

The important factors in the induction of anesthesia by this method are the ischemia of the tissues caused by the pressure of the injected fluid, the compression of the terminal nerve-filaments from the same cause, and the direct paralysis of the sensory nerves by the cocain. The effect of the morphin is not local, but general. Physiologic salt solution is employed as the vehicle, because it is unirritating to the tissues.

The field of operation may be infiltrated *en masse*, or it may be surrounded by an anesthetic edematous zone. In addition, the nerves leading to the part may also be cocainized either some distance from the prospective incision, or directly as they are exposed in the wound. Great care must be taken to avoid injecting the fluid into a bloodvessel.

An ordinary antitoxin syringe capable of holding at least 10 mls may be employed. The derm should be infiltrated before the deeper tissues are injected. The needle having been introduced obliquely, a few drops of the solution are forced out; the needle is then thrust deeper and deeper, while more of the fluid is injected in various directions until the field is thoroughly infiltrated. The subsequent application of an ice-bag to the part will intensify the analgesic effect of the

injection. At least five minutes should elapse after the infiltration before the incision is made. The period of analgesia generally lasts from twenty to thirty minutes. The strength of the solution and the amount employed will depend upon the sensitiveness of the part, the extent of the operation, and the amount of cocain that is likely to be retained in the tissues. It is not safe to allow more than 1 grain of cocain to remain in the part. Of the strong solution, 1 ounce (30.0 mls), of the solution of medium strength, 2 ounces (60.0 mls); and of the weak solution, 10 ounces (300.0 mls) may be employed without risk. Epinephrin increases the anesthetizing power of the cocain, retards its absorption, and decreases bleeding. For infiltration the commercial preparation (1 : 1000) may be used with the cocain solution in the strength of 1 to 50,000.

Medullary Cocainization.—The employment of spinal subarachnoid injections for the purpose of inducing analgesia was suggested by Corning in 1885, and made practical by the researches of Bier, published in 1899. The technic of medullary cocainization is as follows: The entire lumbar and sacral region is prepared with antiseptic care as for operation; the patient is placed in a sitting posture, and the injection is made at the level of the crest of the ilium, that is, just above or below the fourth lumbar vertebra, and 1 cm. ($\frac{1}{3}$ in.) external to its spinous process. The solution is injected through a fine irido-platinum needle, about 9 cm. (3–4 in.) long, attached to an ordinary hypodermic syringe capable of holding 2 mls (30 min.). As the injection should not be made before a flow of cerebrospinal fluid is observed, the needle should be introduced into the subarachnoid space before the syringe is attached. The injection is made very slowly, and to insure the retention of the solution the needle is held *in situ* for about a minute, then carefully withdrawn, and the puncture sealed with collodion. A 2 per cent. solution (9 gr.—1 oz.—0.6 gm.—30.0 mls) of cocain hydrochlorid is usually employed; it should be freshly prepared and sterile. From 15–20 min. (1.0–1.2 mls) are injected. The amount of cocain should not exceed $\frac{2}{5}$ grain (0.025 gm.). Analgesia extending downward from about the level of the diaphragm follows in from five to ten minutes, and usually persists about an hour and a half. It is not accompanied by loss of consciousness.

Spinal analgesia, while useful in special cases, is distinctly dangerous, and the drug once injected is largely beyond the control of the surgeon. The death-rate probably exceeds 1 to 1000 cases. Moreover, it does not cause complete muscular relaxation; it frequently gives rise to unpleasant after-effects—severe headache, vertigo, insomnia, nausea and vomiting, and temporary

paralysis; and in at least 5 or 6 per cent. of the cases it proves wholly unsuccessful. It may be substituted for inhalation anesthesia in pulmonary disease, diabetes, advanced nephritis, and cardiovascular disease. It is not suitable for prolonged, complicated operations, especially if these are intra-abdominal, and, since it does not induce unconsciousness, it should not be employed in young children, nor in insane or hysteric patients. Of late, cocain as a spinal anesthetic has been largely supplanted by less toxic substances, such as tropacocain and stovain. Besides its use as an anesthetic in surgical operations, cocain is extensively employed to relieve pain in various pathological conditions affecting the mucous membranes. In *inflammations* and *ulcerations* of the *nose*, *pharynx* and *larynx* it may be used alone or in combination with antiseptic sprays or powders. In *laryngeal tuberculosis* it is invaluable for relieving the intense pain and dysphagia. It may be applied by insufflation in combination with iodoform. In *acute coryza* and *hay-fever* it gives temporary relief by lessening sensibility and constricting the turgid tissues, but epinephrin is preferable and does not induce a habit. Ointments or suppositories containing cocain are sometimes employed to lessen pain in *anal fissure* and *hemorrhoids*. Solutions of the drug or powders containing it are given internally to control vomiting and allay pain in *ulcerative* and *inflammatory conditions* of the *stomach*. The application of a 10 per cent. solution of cocain hydrochlorid on a pledget of cotton has been found useful in *rigidity* of the *cervix uteri*.

Mydriatic.—Cocain is often employed as a mydriatic to facilitate ophthalmoscopic examination, as its effects last only for a few hours. In solutions of suitable strength for the eye it has little or no effect upon accommodation and, therefore, it cannot be employed as a substitute for atropin or homatropin in determining errors of refraction.

Systemic Use.—Cocain, being antagonistic to morphin in several respects, has been recommended as an antidote in *acute opium-poisoning*. More than $\frac{1}{4}$ grain (0.015 gm.), however, should not be given. The wine of coca, which was recognized in the United States Pharmacopœia of 1900, has been employed as a general tonic, but it is inferior to a number of other remedies, and, moreover, there is always the possibility that if used repeatedly it may lead to the formation of a habit.

Administration.—As a local anesthetic to mucous membranes, the hydrochlorid is employed in solutions varying in strength from 2 to 10 per cent. The mucous membrane of the larynx is less susceptible than that of the nose or throat. On the latter, from 4 to 6 per cent. solutions are usually sufficient.

A solution stronger than 4 per cent. should not be used in the eye on account of the danger of inducing degenerative changes in the corneal epithelium.

Solutions of cocain do not keep well and for this reason they should always be freshly prepared. Prolonged boiling decomposes cocain into methyl alcohol and benzoyl-ecgonin, but solutions may be sterilized by heating to 212° F. for ten minutes without any appreciable loss of strength.

The drug is not well borne by children and women of a neurotic temperament. The danger of causing the habit from the frequent use of cocain in chronic diseases of the nose and throat must never be lost sight of, and under no circumstances should the remedy be placed in the patient's own hands. In tuberculous laryngitis with dysphagia small tablets containing from $\frac{1}{20}$ to $\frac{1}{12}$ grain (0.003–0.005 gm.) of cocain may be allowed to dissolve slowly in the mouth, or the drug may be used in the form of a powder or spray:

℞. Cocainæ hydrochloridi..... gr. xx (1.3 gm.)
 Resorcinolis..... gr. x (0.65 gm.)
 Aquæ..... f ʒj (30.0 mls).—M.
 Sig.—To be used as a spray. (*Tuberculous laryngitis.*)

Incompatibles.—Cocain is incompatible with tannic acid, alkaline carbonates, iodids, borax, and zinc sulphate. It cannot be added to Dobell's solution, since the latter contains borax.

OTHER SENSORY NERVE DEPRESSANTS

Tropacocain Hydrochlorid (Benzoyl-pseudo-tropein) occurs in Javanese coca leaves, but for commercial purposes it is prepared synthetically. It is readily soluble in water and its solutions may be sterilized by boiling. It is somewhat more irritant than cocain, but less toxic, and is a vasodilator rather than a vasoconstrictor, its effect in this respect about neutralizing that of epinephrin. It dilates the pupil, but its mydriatic action is weaker than that of cocain. It is used especially for *spinal anesthesia*, having an advantage over cocain in its relatively low toxicity. The usual dose is from $\frac{1}{2}$ to 1 grain (0.03–0.65 gm.) in 5 per cent. solution.

Betaeucain.—This compound, which chemically is trimethyl-benzoyl-piperidin, is employed in the form of the chlorid (*Betaeucainæ Hydrochloridum*, U. S. P.) or lactate (benzamin lactate). The former is soluble in 30 parts of water and the latter in 5 parts. Betaeucain is much less toxic than cocain, but more irritant, and slightly less effective as a local anesthetic. Moreover, it dilates the vessels and thus favors bleeding. Its vaso-

dilating effect may be overcome by combining it with epinephrin, although the latter decreases its anesthetic power. It has no effect on the pupil. Its solutions may be sterilized by boiling. For surgical purposes a 2 per cent. solution may be used twice as freely as a corresponding concentration of cocain.

Procain (Novocain, Aminobenzoyl-diethyl-amino-ethanol hydrochlorid) occurs as a crystalline powder, soluble in its own weight of water. It is not affected by boiling, but is readily decomposed by alkalis, even alkaline glass. It is much less toxic than cocain, does not affect the arterioles, and is only slightly irritant. Its anesthetic power is somewhat evanescent, but it may be considerably prolonged by the addition of epinephrin. The drug is not readily absorbed from mucous surfaces and therefore must be used hypodermically. For infiltration anesthesia it is one of the best of the substitutes for cocain and may be used twice as freely as the latter without fear of poisoning. The following solution (1:400) may be injected in amounts up to 3 ounces (100 mls) for anesthetizing the field of operation:

Procain	4 gr. (0.25 gm.)
Normal salt solution	3 oz. (100 mls)
Epinephrin (1 : 1000)	5 min. (0.3 mil)

Solutions of 1 : 200 to 1 : 100 may be used for endoneural injections.

Stovain (Benzoyl-ethyl-dimethyl-aminopropanol hydrochlorid) occurs in colorless scales, soluble in their own weight of water. It is much more irritant than cocain and acts as a vasodilator, but it is decidedly less toxic. Its action is not much increased by epinephrin. Solutions may be sterilized by boiling. It is chiefly used for spinal anesthesia, for which purpose it has advantages over cocain in being relatively less toxic and in causing muscular relaxation. Like cocain and tropacocain, however, it is dangerous if allowed to reach the higher centers. The usual dose is 1 grain (0.06 gm.) in 3 to 5 per cent. solution. The following is a satisfactory combination:

Stovain	4 parts
Lactic acid	4 parts
Glucose	5 parts
Distilled water	to make 100 parts

The lactic acid is added to prevent precipitation of the stovain by the cerebrospinal fluid.

Alypin is structurally similar to stovain. It is readily soluble in water. It is used locally on mucous membranes and also by injection for infiltration purposes. It is more irritant than

cocain and dilates the arterioles, but has no effect on the pupil. Injections have not rarely resulted in collapse, asphyxia, and convulsions. A 4 per cent. solution is used in the urethra and eye. For infiltration a 2 to 10 per cent. solution may be used in amounts up to 2 grains (0.13 gm.).

Benzyl Alcohol (Phenmethylo).—This compound is found in balsam of Tolu and other balsams, but for commercial purposes it is prepared synthetically. It is soluble in water up to 4 per cent., and its solutions may be sterilized by boiling. It is an effective local anesthetic, but its penetrating power is somewhat feeble and its action is transitory. It is much less toxic than cocain, non-irritant in the solutions usually employed, and comparatively cheap.

Benzyl alcohol may be used by injection (1 per cent. solution) and by local application to mucous membranes and cutaneous surfaces, but its use by injection has not proved very satisfactory. Macht, who introduced it in 1918, has found a mixture of pure benzyl alcohol with an equal part of chloroform a most efficient anodyne for *toothache*, when introduced on a pledget of cotton into a tooth cavity or applied to an exposed nerve.

Orthoform is the methyl ester of meta-amido-para-oxybenzoic acid. It is a white voluminous powder, without taste, sparingly soluble in water. It has pronounced analgesic, antiseptic and desiccant properties, and for this reason it has been used as an application to painful ulcers. In the form of an ointment (10–20 per cent.) its analgesic effect lasts from ten to twenty hours. The prolonged action of the drug is due in large part to the slowness with which it is absorbed.

Unfortunately orthoform is not altogether free from irritant properties, and its effects should be carefully watched. Brocq, Asam, Yonge, and others have seen extensive erythema, urticaria, eczema, and even gangrene follow its use. A study of the published records indicates that these accidents are more likely to occur from the use of the drug in an ointment than when it is applied directly in the form of a powder.

It has been used successfully as a local remedy in *painful wounds*, in *burns*, especially of the third degree, in *cancerous* and *tuberculous ulcerations*, and in *fissures* and *excoriations* of the mucocutaneous junctions. It has been especially recommended for relieving the pains of *tuberculous laryngitis* and of *fissured nipples*. In the former the powdered drug may be used; in the latter, a saturated alcoholic solution or an emulsion. The following emulsion has been used with good results at the Pennsylvania State Sanatorium at Mont Alto in tuberculous laryngitis:

R. Mentholis.....	gr. xl (2.5 gm.)
Olei amygdali expressi.....	f 3vi (22.5 mils)
Ovi vitelli.....	f 3iv (15.0 mils)
Orthoform.....	3ii (8.0 gm.)
Aquæ destillatæ.....	q. s. ad f 3ii (60.0 mils).—M.

The slight solubility of the drug unfits it for subcutaneous injection. Added to arsenical pastes (orthoform, 1 part; acacia, 1 part; arsenous acid, 2 parts), it materially lessens the painfulness of their caustic action. Its internal use in doses of from 5 to 10 grains (0.3–0.65 gm.) has been recommended in *gastric ulcer* and *cancer*, but Epstein has observed vomiting and collapse after its administration by the mouth.

Orthoform is incompatible with silver nitrate, antipyrin, and bismuth subnitrate.

Benzocain (Anesthesin), which is closely related to orthoform, is also sparingly soluble in water, but readily soluble in oils, alcohol and ether. It is used for the same purposes as orthoform, and has a decided advantage in being much less irritant. For *painful ulcers* and *pruritus ani* 10 to 20 per cent. ointments may be used. In *tuberculous laryngitis* it may be applied by insufflation or as 10 per cent. emulsion.

Phenacain (Holocain) is a synthetic compound related chemically to acetphenetidin (phenacetin). It is employed in the form of the hydrochlorid (1 per cent. solution). It is about as effective as cocain, and more rapidly acting, but it is much more toxic, and, therefore, it is unsuitable for subcutaneous injection. It has proved to be a valuable anesthetic in *ophthalmic surgery*. The instillation into the eye of a few drops of a 1 per cent. solution causes slight burning, which is followed within a minute by anesthesia lasting about 15 minutes. The drug is without effect upon the pupil, ciliary muscle, or corneal epithelium. As it acts so promptly and effectively, it is especially useful in *minor operations on the eye*, such as the removal of foreign bodies. De Schweinitz and others have spoken favorably of its action in *keratitis*.

Apothesine is the hydrochlorid of diethyl-amino-propyl cinnamate. It occurs as white crystals, which are readily soluble in water or alcohol. Its solutions may be sterilized by boiling. It has an action similar to that of procain (novocain), but it is more toxic. It may be used on mucous membranes (1–2 per cent. solution), for infiltration anesthesia (1 per cent. solution), with or without epinephrin (5 drops of 1 : 1000 sol. to the ounce—30 mils—of apothesine solution), and even for spinal anesthesia (30 min.—2 mils—of a 4 per cent. solution). As much as 10 grains (0.6 gm.) has been used subcutaneously

without untoward effects, although collapse has been reported from smaller doses.

Saligenin (Salicyl Alcohol).—This compound has an action similar to that of procain (novocain), but it is much less toxic and its anesthetic effect is more persistent. It may be used for the same purposes and in the same doses as procain.

Quinin and urea hydrochlorid is soluble in its own weight of water. It is the least toxic of all local anesthetics, and the most persistent in its effects, but in solutions of greater strength than $\frac{1}{4}$ per cent. it is decidedly irritant. It has been used chiefly in $\frac{1}{4}$ per cent. solution for *infiltration anesthesia*. Stronger solutions may cause a deposit of fibrin and occlusion of vessels, and thus lead to sloughing.

Magnesium sulphate has been used intraspinally for the production of anesthesia and muscular relaxation in conditions causing *spinal convulsions*, such as strychnin-poisoning and tetanus, but it is dangerous, as the effective dose is but little less than that required to paralyze the respiratory center. The sensory and motor paralysis develops slowly (1 to 2 hours) and lasts 24 to 48 hours. The usual dose is 1 mil of a 25 per cent. solution of the crystalline salt for every 10 kilos (25 pounds) of body-weight. General anesthesia may also be produced by the subcutaneous injection of 1.5 gm. of magnesium sulphate, in 25 per cent. solution, for every kilo of body-weight. Locally, compresses wet with a saturated solution of magnesium sulphate are effective in relieving pain in *erysipelas*, *acute rheumatism*, *orchitis*, and *neuritis*. To prevent rapid evaporation, 10 per cent. of glycerin may be added to the solution.

Chlorbutanol (Chloretone) has a mild analgesic effect when applied to mucous membranes and raw surfaces. It has been used with more or less success, in solution or powder, on *painful ulcers*.

Dionin (Ethyl morphin hydrochlorid) is a useful local analgesic and lymphagogue in certain inflammatory conditions of the eye, such as *ulcerative* and *interstitial keratitis* and *iridocyclitis*. It is employed in aqueous solutions varying from 2 to 5 per cent., the applications being made from 1 to 3 times a day. The solution at first causes burning pain and marked swelling and injection of the conjunctiva, but this effect soon disappears and is followed by analgesia. The eye soon acquires tolerance for the drug, and after a few applications scarcely any irritant effect is observed. As dionin does not produce complete anesthesia, it cannot be substituted for cocain or holocain in operations on the eye.

Phenol (see p. 405) produces numbness when applied to the unbroken skin, but is incapable of causing complete analgesia.

It is extensively employed to allay itching in *jaundice* and various *pruritic skin diseases*, such as *urticaria* and *eczema*. It may be used in the strength of 1 to 2 drams (4.0–8.0 mils) to the pint (0.5 L.) of water.

Aconite (see p. 52).—The tincture of aconite, rubbed into the affected part, is sometimes useful in relieving the pain of *neuralgia* and *lumbago* and in allaying the itching of *chilblains*. Ointments of aconitin (5 to 10 grains to the ounce—0.3–0.6 gm. to 30.0 gm.) have also been prescribed for neuralgia, but owing to the extremely poisonous nature of the drug they have been abandoned. Liniments containing aconite are sometimes employed to allay muscular pains.

Veratrin is an alkaloid obtained from the seed of *Asagrea officinalis*, a bulbous herb growing in Mexico and Central America. The official preparation is a mixture of pure veratrin and a number of other less active alkaloids. It is a white, amorphous, or semicrystalline powder, odorless and intensely acid. It is readily soluble in alcohol, but very slightly so in water.

Veratrin has an action similar to that of aconitin. It was formerly used as an ointment (4 per cent.) in *neuralgia*.

Hydrocyanic Acid, or prussic acid, is employed in medicine only in the form of a 2 per cent. aqueous solution (*Acidum Hydrocyanicum Dilutum*, U. S. P.). This preparation is a colorless liquid with the odor and taste of bitter almonds. The dose is from 1 to 3 minims (0.06–0.2 mil).

Hydrocyanic acid is a general protoplasmic poison. In moderate doses it first stimulates and then powerfully depresses the central nervous system, especially the respiratory, vasomotor and cardio-inhibitory centers in the medulla. It also depresses the heart or its contained motor ganglia, and decreases all metabolic processes. Large doses kill almost immediately, the heart and respiration being arrested simultaneously. After death the blood often retains for a time its bright red color, owing to the formation of cyan-hemoglobin, a compound that is less readily reduced than oxyhemoglobin. Hydrocyanic acid is partially destroyed in the tissues and partially transformed into sulphocyanides, which escape in the urine. Locally applied, even in dilute solution, it produces numbness of the part by depressing the endings of the sensory nerves.

Toxicology.—When death is not immediate, the characteristic symptoms of prussic acid poisoning are a sense of numbness in the mouth, salivation, dyspnea, dilatation of the pupils, infrequent pulse, clonic convulsions, involuntary discharge of urine and feces, unconsciousness, and collapse. Treatment is rarely effectual on account of the very rapid action of the

drug. It consists in artificial respiration and the use of such stimulants as strychnin and atropin. Sodium hyposulphite has also been recommended in order to form an innocuous sulphocyanide.

In the form of lotion hydrocyanic acid is sometimes used to relieve itching in *eczema* and *pruritus* when there is no abrasion of the skin. Internally, it is sometimes of service in relieving *gastralgia* and controlling the pain and vomiting of *gastric ulcer* and *cancer*. It has also been used to allay cough in *advanced pulmonary tuberculosis*. Dilute prussic acid is very prone to decomposition, and, therefore, the preparations on the market vary considerably in their value. The following formulæ will illustrate the manner in which the drug may be prescribed:

℞. Acidi hydrocyanici diluti..... f℥ss (2.0 mils)
Glycerini..... f℥j (4.0 mils)
Aquaë..... q. s. ad f℥ij (60.0 mils).—M.

Sig.—Apply as directed. (*Pruritus*.)

℞. Bismuthi subnitratiss..... ℥ss (15.0 gm.)
Acidi hydrocyanici diluti..... ℥xl (2.5 mils)
Aquaë..... q. s. ad f℥iv (120.0 mils).—M.

Sig.—Shake well. A dessertspoonful before meals. (*Gastric ulcer or catarrh*.)

℞. Codeinæ sulphatis..... gr. iv (0.25 gm.)
Acidi hydrocyanici diluti..... ℥xxxij (2.0 mils)
Syrupi tolutani..... q. s. ad f℥ij (60.0 mils).—M.

Sig.—A teaspoonful every four hours. (*Cough of pulmonary tuberculosis*.)

Menthol (Peppermint Camphor).—Menthol is a stearopten obtained from the essential oil of peppermint. It occurs as colorless prismatic or acicular crystals, having the odor of mint and a camphoraceous taste. It is sparingly soluble in water, but freely so in alcohol, ether, or chloroform. The dose is from 1 to 3 grains (0.06–0.2 gm.), in pills, capsules, or in alcoholic solution.

Menthol is a mild local anesthetic and an antiseptic. It makes a useful application in *frontal headache* and in *neuralgia of the superficial nerves*. For use in these affections it is best dissolved in chloroform or ether. When equal parts of chloral or menthol are heated together in a water-bath, an oily liquid is formed (chloral-menthol), which is efficacious in *toothache*. One part of menthol to 10 of olive oil makes a soothing application for *burns*. Dissolved in collodion in the proportion of 1:4, it forms a useful dressing for *small contusions*. The inhalation of menthol in the form of a vapor or spray affords considerable relief from the disagreeable symptoms of *acute coryza*. The following solution will be found useful in both *coryza* and *acute laryngitis*:

℞. Mentholis..... gr. vj (0.4 gm.)
 Eucalyptolis..... ℥v (0.3 mls)
 Petrolati liquidi..... f ʒj (30.0 mls).—M.

SIG.—To be used as a spray several times a day.

Solutions of menthol, even as weak as 1 per cent., should not be applied to the nose or throat of infants, as they have been known to produce alarming, or even fatal reflex suffocation (Killian, Lublinski, Gomez, Leroux).

A solution of menthol in liquid petrolatum, in the strength of 5 grains (0.3 gm.), gradually increased if necessary, to 20 grains (1.3 gm.) to the ounce (30.0 mls), is often of service in *pruritus vulvæ*.

Internally, menthol is sometimes used in persistent *vomiting* and *gastralgia*, but it is rarely successful.

Camphorated Chloral.—This is a syrupy liquid made by rubbing together equal parts of camphor and hydrated chloral. It is soluble in alcohol, ether, glycerin, and oils, but it is decomposed by water. It is used as a local anesthetic in *neuralgia*, *toothache*, and *pruritus*. In local *pruritus* the following ointment is sometimes efficacious:

℞. Pulveris camphoræ,
 Pulveris chlorali hydrati..... āā ʒj (4.0 gm.)
 Trit. et add.
 Unguenti aquæ rosæ..... ʒj (30.0 gm.).—M.

Ethyl Chlorid (see p. 129).—When applied to the skin in the form of a fine spray ethyl chlorid freezes the tissues and produces transitory analgesia. The drug is usually sold in small glass tubes provided with a lever-spring top. When the lever is depressed the liquid is expelled in the form of a fine spray by the warmth of the hand. Directed on the skin, the spray in a few seconds causes redness and then pallor, with freezing and numbness. Freezing of the tissues beneath the skin must be avoided, as it is likely to result in sloughing.

Ethyl chlorid is a convenient local anesthetic for use in *minor operations* requiring but a single incision or puncture, such as opening boils and aspirating pleural or abdominal effusions. A drawback is the difficulty of cutting into the hardened tissue. This may be avoided by adopting the method suggested by Bradley, which consists in applying the spray so as to form a circle around the area to be incised, care being taken to keep the spray from the center. The width of the frozen area should be at least $\frac{1}{2}$ inch, and there should be at least 1 inch of unfrozen area in the center. If the incision is made as soon as a white crust forms all the way round there is little or no pain, as the freezing has resulted in a nerve-blocking anesthesia.

Ether (see p. 117).—A spray of ether when applied to the skin produces analgesia through refrigeration, but as this drug is not so volatile as ethyl chlorid it is less effective than the latter.

THE ACTION OF DRUGS ON THE SYMPATHETIC OR AUTONOMIC NERVOUS SYSTEM

The sympathetic or autonomic nervous system supplies through its efferent fibers those organs which are not under the control of the will. It is therefore known also as the involuntary or vegetative nervous system. It comprises all the vertebral ganglia, the ciliary, sphenopalatine and otic ganglia, the celiac ganglion, the mesenteric ganglia, as well as numerous other collections of nerve cells in and around the various viscera, such as the cardiac ganglia and the plexuses of Meissner and Auerbach in the wall of the intestine. These ganglia are all connected with each other, and also through the spinal nerves with the cerebrospinal axis. The organs innervated by the autonomic system comprise the smooth muscles of the blood-vessels, viscera, and iris, the cardiac muscles, and the secretory glands. The functions of all these structures, although they may be influenced through the central nervous system, are in a measure independent of it. The autonomic path consists of two neurons: one whose axon emerges from the gray matter of the central nervous system and terminates in a sympathetic ganglion and another whose axon passes from the ganglion to the peripheral organ. The first axon is known as the preganglionic fiber, the second as the postganglionic fiber. After the injection of nicotin into the circulation, stimulation of the preganglionic fibers causes no response, while stimulation of the postganglionic fibers still produces the usual effects. From this it may be inferred that nicotin paralyzes the connections (synapses) of the preganglion fiber with the sympathetic nerve cell.

The entire autonomic nervous system has two well defined divisions, which are affected similarly by nicotin, but are otherwise antagonistic in their physiologic and pharmacologic reactions, one being augmentory and the other inhibitory. One of these divisions is known as the *sympathetic* and the other as the *parasympathetic* division. The nerves of the sympathetic division arise from the middle portion of the spinal cord (first thoracic to fourth or fifth lumbar nerve), and the nerves of the parasympathetic division arise from the midbrain, bulb and sacral cord. Most of the organs have a double innervation, which is antagonistic, stimulation of the sympathetic fibers producing the

opposite effect from that caused by stimulation of the parasympathetic fibers. Thus, sympathetic stimulation of the heart causes acceleration and parasympathetic stimulation (inhibitory fibers of vagus) slowing of the organ.

The *sympathetic division* supplies the pupil-dilator, the cardio-accelerator, the bronchodilator fibers of the vagus, the intestinal inhibitory and the vasoconstrictor nerves.

The *parasympathetic division* supplies the pupil-constrictor (oculomotor) nerve and the cardio-inhibitory, bronchoconstrictor and intestinal augmentor fibers of the vagus.

In some organs the innervation itself or its pharmacologic reaction is exceptional. The *bloodvessels*, for example, respond chiefly to drugs acting on the sympathetic system. The *sweat-glands* respond to drugs acting exclusively on the parasympathetic system, although anatomically their innervation is purely sympathetic. The *intestines* are exceptional in having a reflex mechanism largely independent of the ordinary (extrinsic) autonomic mechanism. The reflex intestinal movements—peristaltic and pendular or rhythmic—are determined mainly by the intrinsic ganglia (plexuses of Auerbach and Meissner), although they can be initiated, increased or abolished by stimuli from the extrinsic nerves. The intrinsic nervous mechanism responds to the common autonomic poisons, but its stimulation results only in acceleration and strengthening of the normal movements and never in tonic contractions, such as are excited by strong stimulation of the vagus endings. The so-called roll movements, or sudden contractions which propel the intestinal contents through long stretches of bowel, are apparently of extrinsic origin, and due to vagus stimulation and depression of sympathetic inhibition.

The sympathetic innervation (hypogastric) of the *uterus* is peculiar in that it reacts not only to sympathetic poisons (epinephrin), but also to parasympathetic poisons (physostigmin atropin), the nature of the response depending in a measure upon whether the organ is gravid or non-gravid.

The important drugs acting exclusively on the *sympathetic division* are:

Epinephrin

Tyramin

Cocain.

The effect of all of these is stimulating.

The important drugs acting exclusively on the *parasympathetic division* are:

Atropin

Physostigmin
Muscarin

Pilocarpin.

Atropin is a parasympathetic paralyzant, while physostigmin, pilocarpin and muscarin are parasympathetic stimulants.

It must be borne in mind that our knowledge of the autonomic nervous system, although it has been much extended by the studies of Gaskell, Langley and others, is still far from being complete.

MYDRIATICS

The size of the pupil is regulated by the unstriped muscle fibers of the iris, of which there are two sets—concentrically arranged constrictor fibers and radiating dilators fibers. Two antagonistic nerves control these muscles: the oculomotor, which when stimulated contracts the pupil through the agency of the constrictor fibers, and the sympathetic, which when stimulated dilates the pupil through the agency of the dilator fibers.

Mydriasis, or dilatation of the pupil, may be brought about in a variety of ways: by paralyzing the oculomotor center in the medulla; by paralyzing the peripheral filaments of the oculomotor nerve; by paralyzing the constrictor muscle of the iris; by stimulating the sympathetic center in the medulla; by stimulating the peripheral fibers of the sympathetic nerve, or by stimulating the radiating muscular fibers of the iris itself.

All mydriatics impair more or less the *accommodative power* of the eye; that is, its power of adjusting itself to vision at different distances. The agency through which the adjustment is effected is the ciliary muscle. In accommodating for near objects this muscle contracts, the suspensory ligament relaxes, and the lens, owing to its inherent elasticity, becomes more convex. Of the mydriatics, *scopolamin*, *atropin*, and *hyoscyamin* are the most powerful *cycloplegics* or paralyzants of the ciliary muscle, and *cocain* and *eucatropin* (*euphthalmin*) are the most feeble.

Another property of mydriatics is their power of *increasing the intraocular tension*, and so favoring the development of glaucoma when a tendency to that affection already exists. Dilatation of the pupil mechanically increases the intraocular pressure by narrowing the angle between the iris and the cornea, thus impeding the escape of humor from the eye through the small openings communicating with the canal of Schlemm. Of the mydriatics, *cocain* and *eucatropin* have the least effect on the intraocular tension.

Mydriatics are employed to facilitate ophthalmoscopic examination, to paralyze accommodation when estimating refractive errors, to rest the iris and to prevent or break loose adhesion in iritis, to enlarge the field of vision in nuclear cataract, when

the periphery of the lens is still clear, and to allay irritation in inflammation of the cornea.

Mydriatics should never be used if there is any evidence of glaucoma, and, as a rule, it is inadvisable to employ them after the forty-fifth year, as when this age is reached accommodation is so weakened that hyperopia ceases to be latent.

The most important local mydriatics are:

Atropin	Hyoscyamin
Homatropin	Cocain
Methylatropin (eumydrin)	Eucatropin (euphthalmin).
Scopolamin (hyoscine)	

Atropin Sulphate (see p. 73).—Atropin dilates the pupil by paralyzing the oculomotor nerve-endings in the sphincter muscle of the iris, and destroys the power of accommodation by paralyzing the nerve-endings in the ciliary muscle. It also increases the intraocular tension. After the instillation into the eye of a drop or two of a solution of atropin—4 grains to the ounce (0.26 to 30.0 mils)—mydriasis begins in fifteen minutes, and attains its maximum in about half an hour. Accommodation is not affected so quickly, paralysis not being complete within an hour and a half. On the other hand, mydriasis persists somewhat longer than the suspension of accommodation. The effect of an atropin solution of the strength indicated does not usually disappear completely for about ten days.

Atropin may be used as a simple mydriatic to *facilitate ophthalmoscopic examination*, but eucatropin (euphthalmin), cocain, and homatropin are as efficient for this purpose and cause less inconvenience to the patient. As it paralyzes accommodation it is a reliable mydriatic for general use in *refraction work*, but many ophthalmologists prefer cycloplegics which have a less persistent action. In *iritis* it is indispensable in preventing and in breaking up adhesions between the iris and the capsule of the lens. In *acute keratitis* it is also very useful in allaying ciliary irritation.

As a simple mydriatic, $\frac{1}{4}$ grain (0.016 gm.) to the ounce (30.0 mils) is sufficient, and the mydriasis from this solution does not last longer than four or five days. As a cycloplegic, a solution of 4 grains (0.26 gm.) to the ounce (30.0 mils) should be instilled into the eye, one drop at a time, three times for at least a day. A solution of the same strength is generally used in *iritis*. In *keratitis* a solution containing 1 to 2 grains (0.065–0.13 gm.) to the ounce (30.0 mils) will be effective.

Homatropin Hydrobromid.—Homatropin is an artificial alkaloid obtained by heating tropin (a component of atropin)

with mandelic acid, in the presence of dilute hydrochloric acid. It is employed in the form of the hydrobromid (*Homatropinæ Hydrobromidum*, U. S. P.), which is freely soluble in water.

Like atropin, it dilates the pupil and paralyzes accommodation. Its action is complete within an hour, and lasts from two to three days. It has an advantage over atropin in the shorter duration of its effects. It is, however, several times more costly than the natural alkaloid. To paralyze the accommodation a solution of 8 to 12 grains (0.5–0.8 gm.) to the ounce (30.0 mls) must be instilled in the conjunctival sac six or eight times at intervals of fifteen minutes. In facilitating ophthalmoscopic examination a solution of 1 to 2 grains (0.06–0.13 gm.) to the ounce (30.0 mls) is sufficient.

Methylatropin or **Eumydrin** has properties similar to those of atropin, though it is not so poisonous. As a mydriatic it acts more quickly than atropin, but its effects are less lasting. It is applied in from 1 to 2 per cent. solution.

Hyoscyamin (see p. 80).—This alkaloid is obtained from *hyoscyamus* and other *Solanaceæ*. It is official in the form of hydrobromid (*Hyoscyaminæ Hydrobromidum*), which is freely soluble in water. Upon the eye hyoscyamin acts like atropin in dilating the pupil and paralyzing the accommodation, but its effects are less lasting, being not more than six or seven days in duration. Some ophthalmologists prefer it to atropin for this reason. It is usually employed in the strength of 2 grains (0.13 gm.) to the ounce (30.0 mls).

Scopolamin or **Hyoscin Hydrobromid** (see p. 80).—This drug dilates the pupil, paralyzes accommodation, and increases intraocular tension in the same way as atropin; but it acts more powerfully and quickly and its effects are of much shorter duration. Its chief drawback is its greater tendency to cause constitutional disturbance. It may be employed in the strength of 2 grains (0.13 gm.) to the ounce (30.0 mls).

Cocain Hydrochlorid (see p. 162).—The instillation into the eye of a few drops of a 4 per cent. solution of cocain causes, in from ten to fifteen minutes, in addition to local anesthesia, pronounced dilatation of the pupil. The mydriasis attains its maximum in about thirty minutes and lasts but for a few hours. It is of peripheral origin, and due to stimulation of the sympathetic nerve-endings. Cocain only slightly impairs accommodation and is without appreciable effect upon the intraocular pressure. In strong solutions it acts injuriously on the corneal epithelium.

As the effect of cocain on the pupil is of short duration, and as it does not seriously disturb accommodation, it is a convenient

mydriatic for *retinal examinations*. In iritis atropin is distinctly preferable on account of its forcible action and lasting effect. The mydriasis induced by cocain is readily overcome by the instillation into the eye of a few drops of a 1 per cent. solution of physostigmin (eserin). Stronger solutions of cocain than 4 per cent. should not be used in the eye on account of the danger of causing degenerative changes in the corneal epithelium.

Eucatropin (Euphthalmin).—This synthetic alkaloid is the hydrochlorid of the mandelic acid derivative of betaeucain. It occurs in the form of a white crystalline powder, soluble in cold water. Its solutions can be sterilized by boiling, and may thus be kept for a long time. If a few drops of a 5 per cent. solution be placed in the conjunctival sac, mydriasis begins in a few minutes, attains its maximum in about half an hour, and passes away within six or seven hours. While its mode of action has not been fully determined, it is probable that the drug dilates the pupil by paralyzing the peripheral ends of the oculomotor nerve. Eucatropin does not injure the corneal epithelium; it does not irritate the conjunctiva; it gives rise to no constitutional disturbance; and it only slightly impairs accommodation. Contrary to what has been stated, however, it does increase to some extent the intraocular tension, and Knapp has observed glaucoma follow the use of a 7.5 per cent. solution. On account of the brief duration of its action on the pupil, and its slight cycloplegic influence, it is perhaps the best agent we possess for *simple ophthalmoscopic purposes*. Solutions varying from 4 to 6 per cent. are usually employed. According to Jackson, the following solution is more active in dilating the pupil and at the same time less persistent in its effect than a stronger solution of eucatropin alone:

Eucatropin.....	1 part
Cocain hydrochlorid.....	1 part
Distilled water.....	100 parts

MIOTICS

Miosis, or contraction of the pupil, may result from causes the reverse of those mentioned as being capable of bringing about mydriasis. *Morphin*, when taken internally in large doses, contracts the pupil by stimulating the oculomotor center. *Physostigmin* and *pilocarpin*, applied directly to the eye, cause contraction of the pupil by stimulating the peripheral endings of the oculomotor nerve. Both drugs also lessen intraocular tension by widening the angle between the iris and the cornea, thus favoring the escape of humor from the eye, and, in strong solution,

induce spasm of accommodation. *Arecolin* apparently has a similar action.

Physostigmin or Eserin Salicylate (see p. 154).—This is the most commonly used miotic. When a gentle, continuous action is desired, a solution containing from $\frac{1}{8}$ to 1 grain (0.008–0.065 gm.) to the ounce (30.0 mls) is sufficient, but when a prompt and powerful effect is required, a solution containing from 2 to 3 grains (0.13–0.3 gm.) to the ounce (30.0 mls) must be used. The miosis reaches its maximum in about half an hour, remains maximal for about three hours, and then gradually subsides, the pupil becoming normal in about three or four days. The miosis, which is due to stimulation of oculomotor endings, is accompanied by spasm of accommodation and a decrease in the intraocular tension, the latter resulting from the miosis, which widens the spaces of Fontana and thus permits a greater quantity of fluid to escape from the anterior chamber into Schlemm's canal.

Physostigmin is especially useful for its effect upon the intraocular tension in *acute* and *subacute congestive glaucoma*. A drop or two of the solution should be instilled into the eye every hour or two. Unless relief is promptly obtained recourse should be had to iridectomy. On standing solutions of physostigmin turn red and lose some of their effectiveness.

Pilocarpin Hydrochlorid (see p. 272).—The action of pilocarpin on the eye is very much like that of physostigmin, but less powerful. It is employed in solution of from 1 to 5 grains (0.065–0.3 gm.) to the ounce (30.0 mls).

Arecolin Hydrobromid.—This is the hydrobromid of a liquid alkaloid obtained from *Areca Catechu*, or betel-nut. It is a white crystalline salt, soluble in water. In the form of $\frac{1}{2}$ or 1 per cent. solution ($2\frac{1}{4}$ – $4\frac{1}{2}$ gr. to the ounce—0.14–0.3 gm. to 30.0 mls) it is a powerful miotic. Contraction of the pupil begins in from three to five minutes, reaches its maximum in from ten to fifteen minutes, and is accompanied by spasm of the ciliary muscle. The pupil returns to its normal condition within an hour or two. Its action is more rapid, but at the same time more transient, than that of physostigmin. Its power of lowering tension in *glaucoma* is apparently equal to that of physostigmin.

Arecolin has been used with asserted success as an anthelmintic, and, according to Frohner and Clemesma, it is, when injected hypodermically, a more powerful sialagogue than pilocarpin.

EMETICS

Vomiting is a reflex act consisting of a forcible spasmodic contraction of the abdominal muscles and diaphragm. While

the contraction of the muscular coat of the stomach may assist in the act, it is not an essential factor, for Magendie found that if the stomach was removed and was replaced by a bladder filled with water emesis could still occur. The afferent impulses which excite vomiting travel from the stomach through the sensory fibers of the vagus to a center in the medulla closely connected with the respiratory center, and thence the efferent impulses are conducted through the phrenics, the spinal nerves, and the vagus to the muscles concerned in the act. Theoretically, a drug may cause vomiting either by directly affecting the center in the medulla or by indirectly affecting it through irritation of the afferent nerve-endings in the stomach. It is not always an easy matter to determine the exact mode of action of an emetic. If the drug be injected into a vein, it may act directly on the vomiting center, or, being eliminated through the stomach, it may act reflexly by irritating the afferent nerves of that organ; or again, if the drug be given by the mouth, it may irritate the stomach and provoke emesis through a reflex action, or, being absorbed, it may excite the vomiting center directly. If, however, a drug acts more promptly when injected intravenously than when it is given by the mouth, and if vomiting follows its injection after the stomach has been replaced by a bladder filled with water, after all the arteries leading to the stomach have been ligated, or after division of both vagi, it may be assumed that its action is chiefly a direct one on the center in the medulla. The action of *apomorphin* is purely central, that of *mustard*, *copper sulphate*, *zinc sulphate*, *alum*, *antimony (tartar emetic)*, and *yellow sulphate of mercury* entirely peripheral, and that of *ippecacuanha* is probably both central and peripheral. Emetics in small doses increase the bronchial secretion and lessen its viscosity; for this reason those that act slowly, such as *ippecacuanha* and *antimony*, are often used as sedative expectorants.

Emetics may be employed for one of two purposes: To expel irritating food or poisons from the stomach, and to expel foreign bodies, false membrane, or excessive secretion from the respiratory tract.

Emetics should be avoided or used with extreme caution in late pregnancy and in persons suffering from aneurysm, advanced arteriosclerosis or hernia.

Apomorphin Hydrochlorid.—This is an artificial alkaloid obtained by abstracting from morphin a molecule of water. It is prepared by maintaining at a high temperature for several hours, in a sealed retort, a mixture (1 : 20) of morphin and strong hydrochloric acid. The hydrochlorid (*Apomorphinæ Hydrochloridum*, U. S. P.) appears as minute grayish-white crystals, having a

faintly bitter taste, and acquiring a greenish tint on exposure to light and air. The dose as an emetic is from $\frac{1}{12}$ to $\frac{1}{8}$ grain (0.005–0.008 gm.) hypodermically; as an expectorant $\frac{1}{30}$ to $\frac{1}{20}$ grain (0.002–0.003 gr.) by the mouth.

In man the subcutaneous injection of $\frac{1}{10}$ grain (0.006 gm.) of apomorphin is followed within fifteen minutes by nausea and vomiting. The emesis is accompanied by muscular relaxation, quickening of the pulse, and an increase in the faucial and bronchial secretions. The vomiting is of central origin.

Apomorphin is employed as an emetic and as a sedative expectorant. The certainty and promptness of its action and its freedom from irritant properties when given hypodermically make it almost an ideal emetic in *poisoning*, especially when swallowing is impossible or the state of the stomach is such as to forbid the use of emetics having a peripheral action. In young children and infirm subjects, however, considerable caution must be exercised in its employment, since its action may be attended with profound prostration or even collapse.

In *acute alcoholism* the drug is especially efficacious. In some cases of narcotic poisoning, on account of the decreased sensitiveness of the medullary center, apomorphin, like other emetics, may prove inefficient. In small doses ($\frac{1}{30}$ gr.–0.002 gm.) the drug has some soporific power, for which it has been especially recommended in *delirium tremens*.

As an emetic, apomorphin should be administered hypodermically, although it will provoke vomiting when given by the mouth, if the dose is sufficiently large. Solutions are most conveniently prepared from tablets containing the requisite dose. Both tablets and solution are liable to deteriorate with age and on exposure to light and air. As an expectorant, apomorphin should be given by the mouth in the form of a solution, pill or capsule. It is incompatible with alkalis, potassium iodid, ferric chlorid and diacetylmorphin (heroin).

Ipecacuanha (see p. 284).—This drug is a safe and fairly prompt emetic. Its action is not so vigorous or so depressing as that of the mineral emetics. It is especially adapted for children, in whom it may be employed to unload the stomach of irritant food or to expel tenacious mucus from the air passages. The syrup and the wine are eligible preparations, and either may be given to children in doses of from $\frac{1}{2}$ to 2 fluid rams (2.0–8.0 mls).

Tartar Emetic (see p. 283).—This drug has been discarded as an emetic because of its slow and very depressant action.

Zinc Sulphate (see p. 366).—As an emetic zinc sulphate is employed chiefly in *narcotic poisoning*. The dose is from

10 to 20 grains (0.65–1.3 gm.), repeated in fifteen or twenty minutes, if necessary.

Copper Sulphate (see p. 365).—This drug is a more prompt and powerful emetic than zinc sulphate. In *phosphorus-poisoning* it serves a double purpose: it not only unloads the stomach, but it also acts as a partial antidote by coating the phosphorus with reduced copper. The dose of copper sulphate is from 5 to 10 grains (0.3–0.65 gm.), and when this amount has been administered without effect, it is best not to repeat it, but to resort to some other emetic.

Mercury Subsulphate (Turpeth Mineral).—This drug was formerly used in doses of 2 to 3 grains (0.13–0.2 gm.) as an emetic in croup. Although certainty, quickness of action, tastelessness, and small bulk are in its favor, it cannot be recommended on account of its exceedingly irritant properties.

Alum (see p. 357).—Powdered alum is a safe but somewhat uncertain emetic. It may be given to children in doses of a teaspoonful in syrup, and repeated once or twice if vomiting does not ensue.

Mustard.—Mustard flour is a prompt and energetic emetic. It may replace zinc sulphate or copper sulphate in *narcotic poisoning*. It is contraindicated when there is acute gastritis. The dose is a tablespoonful stirred up in a glass of water, and repeated in ten or fifteen minutes, if necessary.

ANTI-EMETICS

The treatment of vomiting varies with the cause. In the vomiting of *intestinal obstruction*, it is only in rare instances that any measure short of surgical intervention brings relief. Persistent vomiting may be a symptom of *uremia*, and in this case the chief reliance must be on eliminative measures. *Reflex vomiting* sometimes occurs in association with lesions of the gall-bladder, appendix, uterus, uterine appendages, etc. It can be relieved permanently only by the removal of the underlying condition.

The exact cause of the vomiting of *pregnancy* is still undetermined. Assuming that non-absorption of the corpus luteum is a factor in the milder forms, Hirst has used intramuscular injections of an extract of corpus luteum with some success. In so-called pernicious vomiting of pregnancy, which is apparently due to an autointoxication arising from some obscure derangement of metabolism, careful regulation of the diet, with reduc-

tion or exclusion of protein, mild laxatives, warm baths, and rectal or subcutaneous injections of saline solution may afford relief. If these measures fail, however, and the life of the patient is jeopardized by the incessant vomiting, there should be no question as to the advisability of terminating the pregnancy.

A peculiar form of vomiting is that which is known, for want of a better name, as *nervous vomiting*. It is not associated with any anatomic lesion of the stomach or with changes in the quantity or quality of the food, nor is it apparently of reflex character. In many instances it is evidently a symptom of hysteria. In this condition anti-emetics—cerium oxalate, bismuth subcarbonate, diluted hydrocyanic acid, menthol—may be useful, but more often they fail. Suppositories of valerian, asafetida, etc. may be tried. Gastric lavage, followed by the administration of silver nitrate in small doses, sometimes serves to allay the irritability of the gastric nerves. Sinapisms or hot compresses over the epigastrium are indicated. A spray of ethyl chlorid along the spine and over the stomach has given good results. Galvanism, with one pole (negative) over the back and the other within the stomach, may afford relief. In some cases it is necessary to keep the patient absolutely quiet in the recumbent position, and to feed by the rectum.

Vomiting the result of *gastric carcinoma* is sometimes temporarily relieved by anti-emetics. Cerium oxalate, bismuth subnitrate, diluted hydrocyanic acid, chloroform, and cocain may be tried. If the pylorus is obstructed and the vomiting is the result of abnormal retention of food lavage is indicated. If the vomiting of *peptic ulcer* is not relieved promptly by such sedatives as bismuth subcarbonate, cerium oxalate, silver nitrate, etc., the patient should be kept at complete rest and nourished for a few days by rectal feeding. Counterirritation by means of sinapisms over the epigastrium is often useful.

Nausea and vomiting resulting from *etherization* or *chloroformization* is usually relieved by the administration of cracked ice and of brandy or small doses of acetphenetidin. In refractory cases the stomach should be washed out.

From the foregoing it is evident that while anti-emetics are often of service, they should be regarded as only palliative remedies or as adjuvants to more important curative measures. Anti-emetics may accomplish their purpose directly by acting on the vomiting center in the medulla, or indirectly by protecting the irritated gastric mucosa or reducing the sensitiveness of the nerve-endings in the stomach. To the first class belong:

Morphin

Bromids

Hydrated chloral.

To the second class belong:

Bismuth subcarbonate or subnitrate	Diluted hydrocyanic acid
Cerium oxalate	Silver nitrate
Cocain	Chloroform
Phenol	Carbonated waters
Cracked Ice.	

All of these agents are considered under other headings.

GASTRIC ANTACIDS

Gastric antacids are drugs that neutralize the acidity of the gastric contents. Certain drugs, such as sodium bicarbonate, decrease not only the acidity of the gastric contents, but being excreted as alkalis, also reduce the acidity of the urine; others serve as antacids in the stomach, but being poorly absorbed (magnesium oxid, calcium carbonate) or being excreted as neutral compounds (ammonia), have little effect upon the reaction of the urine; and others still, such as the sodium and potassium salts of the organic acids, have little effect upon gastric acidity, but being excreted in alkaline form (bicarbonates), decrease the acidity of the urine.

It was formerly believed that the mild alkalis, when taken before meals, stimulate gastric secretion, but the studies of Reichmann, Pawlow, Chiari, and others have clearly shown that they have no such effect. What efficacy they have in mild derangements of digestion is to be ascribed to their power of neutralizing excessive acidity, dissolving tenacious mucus, and overcoming pylorospasm, when this is due to abnormal acidity.

In concentrated form alkalis, even the milder ones, decrease the quantity of gastric juice, lessen its acidity, and inhibit the action of pepsin.

Gastric antacids are employed as such to neutralize the organic acids (lactic, butyric, and acetic) resulting from fermentation of the gastric contents, and which excite eructations, heart-burn, and gastralgia; to lessen the acidity in cases of hyperchlorhydria; and to antagonize poisons of an acid character.

The most important gastric antacids are:

Sodium bicarbonate	Magnesium carbonate
Lime-water	Calcium carbonate
Magnesium oxid	Ammonia
Bismuth subcarbonate.	

The strong alkalis—sodium carbonate, sodium hydroxid and potassium hydroxid—are too irritant to be used as gastric antacids.

SODII BICARBONAS, U. S. P.

(Sodium Bicarbonate, Baking Soda, NaCHO_3)

Sodium bicarbonate is a white, opaque, odorless powder, having a cooling, mildly alkaline taste. It is soluble in 10 parts of water and is insoluble in alcohol. The dose is from 5 to 30 grains (0.3–2.0 gm.).

PREPARATION

DOSE

Trochisci Sodii Bicarbonatis, U. S. P.. (3 gr.—0.18 gm. of sod. bicarb. and $\frac{1}{6}$ gr.—0.01 gm. of nutmeg in each).

Therapeutics.—Sodium bicarbonate is extensively used in diseases of the stomach to neutralize abnormal acids or hydrochloric acid when in excess. Given before meals, in small doses (3–5 gr.—0.2–0.3 gm.) with some bitter stomachic, it often affords relief in *mild forms of indigestion of a functional nature*. Given an hour or two after meals, it allays the burning pain, eructations, and palpitation due to the *acids of fermentation*. Given at the height of digestion, in doses of from 10 to 15 grains (0.6–1.0 gm.) it relieves the painful crises of *hyperchlorhydria*. Large doses are also useful in neutralizing the hydrochloric superacidity of *gastric ulcer*, but combination with bismuth subcarbonate, owing to the more persistent effect of the latter, is preferable to sodium bicarbonate alone. In the *chronic gastro-intestinal catarrh of childhood*, characterized by a capricious appetite, tympanites, eructations, troubled sleep, and hard, lumpy, mucous stools, sodium bicarbonate with a bitter and a mild laxative often gives excellent results.

In *diabetes mellitus with acetone bodies in the urine* sodium bicarbonate in large doses is of value in averting coma. The amount required varies from 6 to 12 drams (25.0–50.0 gm.) daily. When coma is impending or has actually developed the drug should be given not only by the mouth or rectum, but also intravenously (500 mls of a 4 per cent. solution, made with freshly sterilized water, every few hours). A neutral reaction of the urine, or, better, a normal blood CO_2 reading, is an indication that sufficient alkali has been given. The reaction of the urine is not wholly reliable, for if the function of the kidneys is impaired, the urine may not become alkaline until the blood bicarbonate reserve is far in excess of normal. Overdoses of sodium bicarbonate in cases of acidosis may result in alkalosis and the occurrence of tetany.

Sodium bicarbonate and other alkalis are commonly employed in conjunction with salicylates in *rheumatism*. While they probably have no influence on the disease itself, they tend to prevent the formation of salicylic acid, which is irritant to the stomach.

For neutralizing the urine in *pyelitis*, *cystitis*, etc. the salts of the vegetable acids, such as citrates and acetates, are preferable to sodium bicarbonate, as their action in the stomach is neutral.

Sodium bicarbonate is sometimes used externally as a sedative dressing in *superficial burns*. A 5 to 10 per cent. solution is an excellent remedy for *thrush*. It is employed as a detergent in many washes designed for *chronic catarrhal affections of the nasopharynx*, and it is an ingredient of the well-known Dobell's solution, which may be prescribed as follows:

R.	Sodii bicarbonatis	
	Sodii boratis.....	āā 3j (4.0 gm.)
	Phenolis.....	gr. xxx (2.0 gm.)
	Glycerini.....	f 3j (30.0 mls)
	Aquæ.....	Oij (1.0 L).—M.

Untoward Effects.—Large doses in concentrated solution may cause nausea and vomiting. In diabetic acidosis massive doses may produce edema by causing a retention of chlorids in the body with a resultant retention of water. Cases have been reported also in which the drug was given in such large quantities that, before the urine became alkaline, a state of alkalosis with tetany supervened.

Administration.—In simple hyperchlorhydria and gastric ulcer with hyperacidity, sodium bicarbonate should be given about an hour or an hour and a half after meals and preferably in combination with more slowly acting antacids, such as magnesium oxid and bismuth subcarbonate.

R.	Sodii bicarbonatis.....	3iiss (10.0 gm.)
	Magnesii oxidi.....	3iii (12.0 gm.)
	Bismuth subcarbonatis.....	3iii (12.0 gm.).—M.

Fiant chartulæ No. xx.

Sig.—One powder an hour after meals.

Large doses of sodium bicarbonate, such are sometimes required in diabetes, are less likely to cause nausea and vomiting if taken in large draughts of carbonated water. Solutions intended for intravenous use should not be boiled, as the heat tends to transform the bicarbonate into the irritant carbonate. Subcutaneous injections should be avoided, as they not rarely cause sloughing of the tissues.

Incompatibles.—Sodium bicarbonate is incompatible with acids, metallic salts and alkaloids.

LIQUOR CALCIS, U. S. P.

(Solution of Calcium Hydroxid, Lime-water)

Lime-water is a saturated aqueous solution of calcium hydroxid made by slaking lime with water. It is a clear, colorless liquid, odorless, and having a saline, slightly caustic taste. It contains about 0.17 per cent. of calcium hydroxid. The dose is from $\frac{1}{2}$ to 2 fluidounces (15.0–60.0 mls).

PREPARATIONS

Linimentum Calcis, U. S. P. (lime liniment, Carron oil), contains equal volumes of lime-water and linseed oil.

Lotio Hydrargyri Flava (yellow-wash), $\frac{1}{2}$ dr. (2.0 gm.) of corrosive sublimate to 1 pint (0.5 L.) of lime-water.

Lotio Hydrargyri Nigra (black-wash), 1 dr. (4.0 gm.) of calomel to 1 pint (0.5 L.) of lime-water.

Therapeutics.—In all conditions in which cows' milk is the chief article of diet, lime-water may be added to the milk to prevent the formation in the stomach of hard curds. In the *diarrhea of children* and in *typhoid fever* it is especially useful when employed in this way. It is sometimes a useful remedy in *obstinate vomiting*, particularly when the latter is due to a high degree of acidity. In *chronic gastric catarrh* with excessive secretion of mucus, washing out the stomach with a weak solution of lime-water (1:5) before breakfast may be practised with benefit.

Inhalations of atomized lime-water have been recommended for their solvent effect in *diphtheria* and *fibrinous bronchitis*. As an alkaline astringent lime-water is sometimes employed as an injection in *vaginitis*, *leucorrhea*, and *urethritis*. It may be used also as an injection in *seat-worms*, although it is inferior to an infusion of quassia. Carron oil is used as a soothing application for *burns* and *scalds*. It has received its name from being so extensively used by the workmen in the foundries at Carron, Scotland.

OTHER ANTACIDS

Magnesium Oxid (see p. 235).—Magnesia or magnesium oxid is official in two forms: light or calcined magnesia (*Magnesii Oxidum*) and heavy magnesia (*Magnesii Oxidum Ponderosum*). Both forms occur as a white, insoluble powder, odorless, and having a slightly earthy taste. Heavy differs from light magnesia not only in its weight, but also in its not readily uniting with water to form a gelatinous hydroxid. The dose of either oxid is from 10 to 60 grains (0.65–4.0 gm.).

Compared with sodium bicarbonate, the antacid action of magnesium oxid is less prompt, but four times more powerful

and much more prolonged. The drug also combines the usefulness of an antacid with that of a mild laxative. When there is constipation, it may be given instead of sodium bicarbonate or combined with that drug in all conditions in which an antacid is indicated. In the *diarrhea* of childhood, when there is unnatural acidity of the digestive tract, it is an excellent laxative for removing sour, indigestible food. In *ulcer of the stomach* it may be advantageously combined with bismuth subcarbonate and sodium bicarbonate.

Magnesium Carbonate (see p. 235).—This drug may be used in the same doses and for the same purposes as magnesium oxid, but as it liberates large quantities of CO_2 gas in the presence of high acidity, the latter is preferred.

Calcium Carbonate (see p. 377).—Calcium carbonate or chalk is an unirritating antacid and a feeble astringent. It is very useful in *diarrhea* with acidity of the digestive tract, and it may be combined with bismuth subcarbonate in the treatment of *gastric ulcer* when there is a marked tendency to looseness of the bowels. It is a chemical antidote to all the *poisonous acids*.

Bismuth Subcarbonate (see p. 376).—This compound has only one-third of the neutralizing power of sodium bicarbonate, but its action is gradual and prolonged. Moreover, it combines the properties of a gastric antacid with those of a protective. In many cases of *hyperchlorhydria* it may be combined advantageously with magnesium oxid or sodium bicarbonate.

Ammonia (see p. 282).—Aromatic spirit of ammonia, in doses of from 20 to 30 minims (1.3–2.0 mls), may be used instead of sodium bicarbonate to relieve the headache, heart-burn, and pyrosis arising from acid fermentation in the stomach. Owing to its stimulating properties, it is inferior to sodium bicarbonate, magnesium oxid and bismuth subcarbonate in *hyperchlorhydria*.

STOMACHICS

Stomachics are drugs that improve the appetite. The most important are:

Gentian	Condurango
Quassia	Taraxacum
Calumba	Eupatorium
Nux vomica	Serpentaria
Cinchona	Wild cherry
Chirata	Hydrastis
Chamomile	Alcohol.

All of these remedies, with the exception of alcohol, owe their activity to a bitter principle. Taken by the mouth bitters improve the appetite, and, by stimulating the gustatory nerve-endings, reflexly increase the salivary and, probably, gastric secretions. With the exception of *nux vomica* and *cinchona*, which have important systemic actions, they exert no direct influence beyond the digestive organs. To be effective they should be taken in liquid form, with the bitter taste undisguised, a short time before meals. As a class, stomachics are useful in atony of the stomach, in chronic gastritis, if the mucous membrane of the stomach is not very irritable, and in the early stages of gastric carcinoma. They should be avoided in all conditions characterized by pronounced irritability of the gastric mucous membrane or by gastric hypersecretion.

GENTIANA, U. S. P.

(Gentian)

Gentian is the root of *Gentiana lutea*, a perennial herb growing in the mountainous districts of Central and Southern Europe. It contains the bitter glucosides *gentiin* and *gentiamarin* and a small amount of *tannin*.

PREPARATIONS

DOSE

Tinctura Gentianæ Composita, U. S. P.	} 1-2 fl. dr. (4.0-8.0 mls)
(contains also bitter orange-peel and cardamom)	
Fluidextractum Gentianæ, U. S. P.....	10-30 min. (0.6-2.0 mls)
Infusum Gentianæ Compositum.....	$\frac{1}{2}$ -1 fl. oz. (15.0-30.0 mls)
Extractum Gentianæ, U. S. P.....	2-5 gr. (0.13-0.3 gm.).

Therapeutics.—Gentian is one of the most reliable of the simple bitters. It is often of value in indigestion due to *atony of the stomach* or *mild gastric catarrh*. A combination with a mild alkali, such as the following is usually effective:

R. Sodii bicarbonatis..... ʒij (8.0 gm.)
 Infusi gentianæ compositi..... f ʒvj (180.0 mls).—M.
 Sig.—A tablespoonful before meals.

In the subacid form of chronic gastritis, however, a combination with hydrochloric acid, such as the following is to be preferred:

R. Tincturæ nucis vomicæ..... f ʒii (8.0 mls)
 Acidi hydrochlorici diluti..... f ʒiiss (10.0 mls)
 Tincturæ gentianæ compositæ q. s. ad f ʒiii (90.0 mls).—M.
 Sig.—One teaspoonful in a wineglassful of water before meals.

QUASSIA, U. S. P.

Quassia is the wood of *Picrasma excelsa*, or of *Quassia amara*, a tree resembling the common ash, growing in the West Indies. It contains a bitter crystalline principle, *quassin*, but no tannic acid. The dose of quassin is from $\frac{1}{30}$ to $\frac{1}{3}$ grain (0.002–0.02 gm.).

PREPARATIONS

DOSE

Tinctura Quassiæ, U. S. P.	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mils)
Infusum Quassiæ.	$\frac{1}{2}$ –1 fl. oz. (15.0–30.0 mils).

Therapeutics.—As a stomachic, quassia may be used in the same class of cases as gentian.

The rectal injection of an infusion made by adding an ounce (30.0 gm.) of quassia chips to a pint (0.5 L.) of water is an efficient anthelmintic against *seat-worms*. To secure the best results the bowel should first be thoroughly cleansed by means of a simple soap-and-water enema.

As quassia does not contain tannin, its preparations are not incompatible with the salts of iron.

CALUMBA, U. S. P.

(Columbo)

Calumba is the root of *Jateorhiza palmata*, growing in Eastern Africa. It contains an alkaloid, *berberin*, a neutral principle, *columbin*, and *columbic acid*, all of which are bitter.

PREPARATIONS

DOSE

Tinctura Calumbæ, U. S. P.	$\frac{1}{2}$ –2 fl. dr. (2.0–8.0 mils)
Infusum Calumbæ.	$\frac{1}{2}$ –1 fl. oz. (15.0–30.0 mils).

Therapeutics.—Calumba is a pure, unirritating bitter, and may be prescribed with confidence in the various conditions in which stomachics are indicated. It may be combined with either acids or alkalis, and since it contains no tannin, it does not form a black, unsightly mixture with the salts of iron. In *atony of the stomach* it may be combined with *nux vomica*, as in the following formula:

R. Tincturæ capsici. ℥xvj (1.0 mil)
 Tincturæ nucis vomicæ. f ʒij (8.0 mils)
 Tincturæ calumbæ. q. s. ad f ʒij (60.0 mils).—M.
 Sig.—A teaspoonful in water before meals.

CHIRATA

(Chiretta)

Chirata is the entire plant of *Swertia chirayita*, growing in the mountains of Northern India. It contains a bitter crystalline glucosid, *chiratin*, and *ophelic acid*, which is also bitter.

PREPARATIONS	DOSE
Fluidextractum Chirataë.....	10-30 min. (0.6-2.0 mils)
Tinctura Chirataë.....	$\frac{1}{2}$ -1 fl. dr. (0.2-4.0 mils)
Infusum Chirataë.....	$\frac{1}{2}$ -1 fl. oz. (15.0-30.0 mils).

Therapeutics.—Chirata is a simple bitter and may be used in the same class of cases as gentian. Like quassia and calumba, it is free from tannin; it is therefore not incompatible with iron salts.

ANTHEMIS

(Chamomile)

Chamomile is the flower-heads of *Anthemis nobilis*, a perennial plant cultivated in Western Europe, and to some extent in the United States. It contains a volatile oil, a bitter principle, *anthemin*, and a small amount of tannin. Chamomile is a mild stomachic and carminative, and is usually employed in the form of an infusion (unofficial), of which 1-2 fl. oz. (30.0-60.0 mils) may be given.

CONDURANGO

Condurango is the bark of *Marsdenia Condurango*, a climbing vine indigenous to Ecuador. It contains tannin and one or two bitter glucosids. It is usually employed in the form of the fluid-extract in doses of from 20 to 60 minims (1.2-4.0 mils).

Therapeutics.—Condurango was first recommended by Friedreich in 1874 as a curative remedy in carcinoma of the stomach. Later, Immermann and Riess reported cases in support of this view; but the testimony of numerous impartial observers has proved conclusively that the drug is without specific action. Notwithstanding the adverse opinion as to its curative power, nearly all who have used the drug agree that it often acts beneficially on the concomitant catarrh, sharpening the appetite, lessening the pain, and promoting digestion. In some cases of *simple gastric catarrh* it is also efficacious. It may be prescribed with hydrochloric acid, as in the following formula:

℞. Acidi hydrochlorici diluti..... f ʒiss (6.0 mils)
 Fluidextracti condurango
 Glycerini..... āā f ʒvj (22.5 mils)
 Vini exrici.....q. s. ad f ʒiv (120.0 mils).—M.
 Sig.—A dessertspoonful in water after meals.

TARAXACUM, U. S. P.

(Dandelion)

Taraxacum is the root of *Taraxacum officinale*, growing in Europe and North America. It contains a crystalline bitter principle, *taraxacin*.

PREPARATIONS

DOSE

Fluidextractum Taraxaci, U. S. P.	$\frac{1}{2}$ –2 fl. dr. (2.0–8.0 mils)
Extractum Taraxaci, U. S. P.	5–20 gr. (0.3–1.3 gm.).

Therapeutics.—Taraxacum is a mild stomachic, possessing feeble laxative properties.

EUPATORIUM

(Boneset, Thoroughwort)

Eupatorium is the leaves and flowering tops of *Eupatorium perfoliatum*, a perennial plant growing in North America. It contains a bitter crystalline glucosid, *eupatorin*, tannin, and a volatile oil.

PREPARATIONS

DOSE

Fluidextractum Eupatorii.	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mils)
Infusum Eupatorii.	1–2 fl. oz. (30.0–60.0 mils).

Therapeutics.—Eupatorium is employed as a stomachic and diaphoretic. Large doses excite vomiting and purging. The infusion, taken while hot, has long been a popular household remedy in “colds,” *myalgia*, and *acute amenorrhea due to cold*.

SERPENTARIA, U. S. P.

(Virginia Snakeroot)

Serpentaria is the rhizome and roots of *Aristolochia Serpentaria*, a perennial herb growing in the woods of the Eastern and Southern United States. It contains a bitter principle, *aristolochin*, a resin, tannin, and a volatile oil.

PREPARATIONS

DOSE

Tinctura Cinchonæ Composita, U. S. P., contains 2 per cent. serpentaria.	1–2 fl. dr. (4.0–8.0 mils)
Infusum Serpentariæ.	$\frac{1}{2}$ –1 fl. oz. (15.0–30.0 mils).

Therapeutics.—Serpentaria is believed to possess, in addition to its properties as a bitter tonic, the power of increasing the secretions, especially the sweat and the urine. Large doses are capable of causing nausea and vomiting. Serpentaria has been employed as a stomachic in *atony of the stomach*, and, combined with more potent remedies, such as *nux vomica* and *cinchona*, as a tonic in the convalescent stage of *acute fevers*.

PRUNUS VIRGINIANA, U. S. P.

(Wild Cherry)

Prunus virginiana is the bark of *Prunus serotina*, a large tree growing in North America. It contains tannin, a bitter principle,

a non-crystalline glucoside—*amygdalin*, and a ferment—*emulsin*. Hydrocyanic acid is formed from the interaction of the last two constituents in the presence of water.

PREPARATION

DOSE

Syrupus Pruni Virginianæ, U. S. P.. 1–2 fl. dr. (4.0–8.0 mls).

Therapeutics.—Wild cherry is a bitter tonic and a feeble nerve-sedative. It has been employed in *pulmonary tuberculosis* to allay irritable cough, its efficacy being attributed to the hydrocyanic acid. The amount of acid present, however, is so small that it can scarcely be of therapeutic value. On account of its agreeable taste the syrup is largely used as a *vehicle* for unpalatable drugs.

OTHER STOMACHICS

Alcohol (see p. 130).—In small quantities dilute alcohol augments the flow of the gastric secretion, stimulates the peristaltic movements, and accelerates absorption. Large amounts retard digestion. In the form of a light wine or diluted spirit it is of service in *indigestion due to simple atony of the stomach*, occurring during convalescence from acute illness or developing as a primary condition in old persons, but caution is necessary in prescribing it owing to the danger of inducing a habit. All alcoholic preparations are contraindicated when there is hyperesthesia of the stomach or hypersecretion of acid.

Nux Vomica (see p. 148).—On account of its general tonic properties *nux vomica* has a decided advantage over many other bitters. It not only sharpens the appetite and increases secretion, but it probably has more effect than any other stomachic on the muscular movements of the stomach and intestines. In *chronic indigestion*, if there are no evidences of irritation, it is often very efficient. In *dilatation of the stomach*, the result of *atony of the gastric muscle*, it may be given in large doses.

Cinchona (see p. 445).—Cinchona to a certain extent shares with *nux vomica* the advantage of being a general tonic as well as a stomachic. The compound tincture of cinchona (Huxham's tincture) is specially serviceable as a bitter tonic in the *convalescence of acute febrile diseases*. It may often be advantageous to combine it with *nux vomica*.

Hydrastis (see p. 271).—*Hydrastis* is a useful bitter tonic in *asthenic gastritis* with motor insufficiency. It may be given in the form of the fluidextract, in doses of 10 to 30 minims (0.6–2.0 mls) or of the tincture, in doses of $\frac{1}{2}$ to 1 fluidram (2.0–4.0 mls).

DIGESTANTS

Of the agents which take part in the process of natural digestion the most important from the viewpoint of the therapist are hydrochloric acid, pepsin, and the enzymes contained in the pancreatic secretion—trypsin, amylase, and steapsin. *Hydrochloric acid*, the natural acid of the stomach, is the most valuable of all digestants. It aids digestion not only directly, but also indirectly by favoring secretion, by regulating the action of the gastric sphincters, by preventing fermentation, and by assisting in the conversion of propepsin into the active pepsin and of prorennin into the active rennin. As an aid to digestion it is indicated only in conditions associated with in acidity or marked hypoacidity.

Pepsin, being absent from the gastric juice much less frequently than hydrochloric acid, is distinctly less useful as a remedy than the latter. It may be of service, however, in conditions associated with apepsia or hypopepsia, such as the advanced stages of chronic gastritis, atrophy of the gastric glands, and carcinoma.

Of the *pancreatic enzymes*, trypsin digests proteins, amylase converts starches into sugar, and steapsin splits and saponifies fats. Since these enzymes act best in alkaline or neutral solutions, and the contents of the stomach are naturally acid, it is argued by some authorities that artificial pancreatic extracts can possess no medicinal value; but it should be remembered that the contents of the stomach do not normally become acid until from ten to fifteen minutes after the ingestion of the food, that in indigestion the secretion of acid is often delayed, and that at least one of the constituents of the pancreatic secretion—trypsin, a more powerful proteolytic enzyme than pepsin—retains its effectiveness even in solutions that are slightly acid.

The digestants in common use are:

Hydrochloric acid	Pancreatin	Pepsin.
Diastase	Papain	

ACIDUM HYDROCHLORICUM, U. S. P.

(Hydrochloric or Muriatic Acid, HCl)

The official acid is a colorless, fuming liquid, of a pungent odor and an intensely acid taste. It contains from 31 to 33 per cent. by weight of absolute hydrochloric acid.

PREPARATION

DOSE

Acidum Hydrochloricum Dilutum, U. S. P., contains 10 per cent. of absolute hydrochloric acid.....

5-20 min. (0.3-1.2 mls).

Toxicology.—In overdoses, hydrochloric acid, like other mineral acids, acts as a caustic poison, causing intense burning pain, vomiting and purging of mucous and bloody material, and collapse. The *treatment* consists in neutralizing the acid by soda, lime, chalk, soap, or other alkalis; in protecting the stomach by demulcents; in combating collapse with diffusible stimulants, administered hypodermically; and in relieving pain with morphin.

Therapeutics.—Hydrochloric acid is useful in certain conditions of the stomach associated with in acidity or hypo-acidity, such as *chronic asthenic gastritis*, *atrophy of the gastric glands*, and *carcinoma of the stomach*. It is contraindicated, even though the normal acid is wanting, when there is any evidence of active inflammation. In the *continued fevers* it sometimes acts beneficially as an aid to digestion, the gastric juice in these cases often being deficient.

Administration.—In indigestion the acid should be given after meals, well diluted, care being taken to rinse the mouth thoroughly after its exhibition. It may be prescribed with a bitter tonic, as in the following formula:

R. Strychninæ sulphatis..... gr. j (0.065 gm.)
 Acidi hydrochlorici diluti..... f ʒij (8.0 mls)
 Pepsini ʒiiss (6.0 gm.)
 Tincturæ cardamomi compositæ... f ʒss (15.0 mls)
 Aquæ..... q. s. ad f ʒiv (120.0 mls).—M.
 Sig.—A teaspoonful in water after meals.

Incompatibles.—Hydrochloric acid is incompatible with oxids, alkalis, carbonates, and hydrates, with many metallic salts, with albumin, and with some glucosids (glycyrrhizin). In the above formula the hydrochloric acid sets free insoluble carminic acid, but its formation is of no importance.

PEPSINUM, U. S. P.

(Pepsin)

Pepsin is a proteolytic ferment obtained from the glandular layer of fresh stomachs from healthy pigs. To be up to the official standard, it should be capable of digesting, under favorable conditions, not less than 3000 times its own weight of freshly coagulated and disintegrated egg-albumen. It occurs as a yellowish-white, amorphous powder, or as yellow translucent scales, having a faint odor and slightly acidulous or saline taste. It is soluble in about 50 parts of water, more so in water containing hydrochloric acid, and is insoluble in alcohol. The dose is from 5 to 20 grains (0.3–1.3 gm.).

Therapeutics.—Pepsin is sometimes of service in *chronic gastritis*, *atrophy of the gastric glands*, and *carcinoma of the stomach*,

but, as a rule, it is less efficacious than pancreatin, and both are inferior to dilute hydrochloric acid and bitters. Care should be taken to secure a reliable preparation. Pepsin should be given in full doses, with hydrochloric acid, after meals.

Most substances destroy or impair the proteolytic action of the drug, especially alcohol and alkalis.

PANCREATINUM, U. S. P.

(Pancreatin)

Pancreatin is a mixture of enzymes naturally existing in the pancreas of warm-blooded animals, and usually obtained from the fresh pancreas of the hog or ox. It appears as a yellowish-white, amorphous powder, having a faint odor and a meat-like taste. To be up to the official standard it should be capable of converting not less than 25 times its own weight of starch into substances soluble in water. The dose is from 5 to 20 grains (0.3–1.3 gm.).

In faintly alkaline solution pancreatin has the power of emulsifying fats, and of converting proteins into diffusible peptones, and starches into sugars. In the presence of more than traces of mineral acids or large amounts of alkalis it soon becomes inert.

Pancreatin is extensively used for peptonizing milk and other foods, the process being as follows: Mix 5 grains (0.3 gm.) of pancreatin and 20 grains (1.3 gm.) of sodium bicarbonate in a small tea-cupful of cool water, and pour into a bottle containing a pint (0.5 L.) of fresh milk. Place the bottle in water so hot that the hand can be held in it without discomfort for a minute. As thoroughly digested milk has an unpleasant bitter taste, it is well to arrest digestion at the end of fifteen or twenty minutes by raising the milk for a few seconds to the boiling-point or by placing the bottle on ice.

Pancreatin is a useful aid to digestion in conditions associated with *hypoacidity*. It should be combined with sodium bicarbonate and given immediately before or during meals, so that its digestive powers can be exercised in the stomach before the contents become distinctly acid.

DIASTASE

Diastase is an amylolytic ferment obtained from malted grain—wheat, barley, oats, and rice. It is a yellowish-white or brownish-yellow amorphous powder, tasteless, soluble in water, but insoluble in alcohol. One part, under favorable conditions, should convert 2000 parts of starch into dextrin and maltose. The dose is from 3 to 5 grains (0.2–0.3 gm.).

Extracts of malt containing a variable quantity of diastase are extensively employed. They are marketed in 3 forms: A thin liquid closely resembling beer; a thick brown, syrupy liquid, containing much saccharine material; and a dry powder containing in addition to diastase, dextrin, dextrose, and the salts of barley. These extracts are used as digestants and as general tonics, but their value has been much overrated.

Chittenden finds that although diastase will act in neutral or alkaline solutions, it is most effective in solutions that are slightly acid. It may be given before meals when there is difficulty in digesting starchy foods.

PAPAIN

(Papayotin, Papoid, Caroid)

Papain is an albuminous ferment obtained from *Carica Papaya*, true papaw, or melon tree, growing in the tropics. It is a grayish-white amorphous powder, tasteless, and without odor. It is quite soluble in water and glycerin, but insoluble in alcohol and ether. The dose is from 5 to 10 grains (0.3–0.6 gm.).

It is claimed for papain that it will convert proteins into peptone, starch into maltose, and emulsify fats; and that, although it will act in neutral or acid solutions, it is most active in solutions of an alkaline reaction. Clinical experience with the preparations on the market indicates that the drug is of doubtful value.

CARMINATIVES

Carminatives are drugs that aid in the expulsion of gas from the stomach or intestines. The origin of the word is somewhat obscure; it is probably derived from *carmen*, a card for wool, that is, a cleanser, but according to some authorities it is derived from *carmen*, a charm. The gases found in the alimentary canal are swallowed with the food, are formed by the action of acid upon the carbonates contained in the saliva and food, or they are generated through fermentation or putrefaction of food. The most common cause, however, of abnormal accumulation of gas is fermentation. Excessive accumulations of flatus distend the viscus, and thus occasion distress or actual pain. It has generally been assumed that carminatives favor the escape or onward movement of gases by relaxing the gastric and intestinal musculature, but the studies of Plant favor the view that they operate by stimulating tonus and rhythmic contractions, thus increasing muscular activity. In the form of abdominal disten-

tion that occurs after surgical operations or in severe infections, especially pneumonia or typhoid fever, and which is due to paresis of the gastric and intestinal musculature rather than to excessive formation of gas, carminative oils are much less useful than the more powerful stimulants of smooth muscle, such as physostigmin and pituitary extract. Although carminatives are chiefly valuable in expelling gas already formed, they also possess the power, to a very limited extent, of preventing the formation of flatus, for by quickening the gastric circulation and probably by increasing glandular activity, they play the part of stomachics, thus aiding digestion and lessening fermentation.

Carminatives are also of service in preventing the griping pains that purgatives often induce when administered alone.

With the exception of alcohol, ether, and chloroform, carminatives are aromatics containing volatile oils as their chief active ingredients. The most important drugs of this class are:

Capsicum	Ginger	Fennel
Pepper	Cinnamon	Coriander
Peppermint	Cajuput	Asafetida
Spearmint	Anise	Ether
Cardamom	Pimenta	Compound spirit of
Cloves	Sassafras	ether
Nutmeg	Caraway	Chloroform.
	Oil of turpentine	

Carminatives are usually administered by the mouth, but asafetida and oil of turpentine are often efficacious in removing intestinal flatus when administered in the form of enemata.

CAPSICUM, U. S. P.

(Cayenne Pepper, African Pepper)

Capsicum is the dried fruit of *Capsicum frutescens*, a small shrub growing in tropical America, in Asia, and in Africa. Its active principle is probably *capsaicin*, which appears in the form of colorless crystals of an exceedingly pungent character. The dose of the powdered drug is from 1 to 3 grains (0.06–0.2 gm.).

PREPARATIONS

DOSE

Tinctura Capsici, U. S. P.....	5–15 min. (0.3–1.0 mil)
Oleoresina Capsici, U. S. P.....	¼–1 min. (0.016–0.06 mil)
Emplastrum Capsici, U. S. P.	

Pharmacologic Action and Therapeutics.—Externally applied, capsicum excites burning and redness, and in concentrated form even vesication. When taken internally in small doses, it produces a sense of warmth in the stomach, stimulates

peristalsis, and aids in the expulsion of flatus. Large doses produce severe irritation of the gastrointestinal and genito-urinary tracts, characterized by pain, vomiting, purging, and dysuria, with scanty, dark-colored urine. It is employed chiefly as a rubefacient, stomachic, and carminative. In the form of a liniment it is sometimes useful in *wry-neck*, *myalgia*, and *sprains*. Capsicum plaster is an efficient counterirritant in *pleurodynia* and *bronchitis*. Combined with cantharides (tincture of cantharides, tincture of capsicum, and alcohol, of each, $\frac{1}{2}$ fl. oz.—15 mils) it is frequently employed as a stimulating lotion in *alopecia areata*. A gargle consisting of half an ounce (15 mils) of the tincture in half a pint (235 mils) of water has been much used in domestic medicine in *sore throat* with relaxation of the uvula, but the remedy is inferior to many others, and in severe inflammations it is likely to do harm.

In the *gastric catarrh* following an alcoholic debauch, and characterized by fetid breath, a heavily furred tongue, anorexia, nausea, and a sensation of weight in the epigastrium, the tincture of capsicum in ten-drop doses is an efficient stomachic. In the *flatulent dyspepsia* of the aged, especially of old gourmands, it is a useful adjuvant to other stomachics. Cayenne pepper in small doses may be employed to promote the absorption of certain drugs, notably of quinin. In *obstinate constipation* due to deficient peristalsis a small amount of the oleoresin may be added advantageously to a cathartic pill.

PIPER, U. S. P.

(Black Pepper)

Black pepper is the unripe fruit of *Piper nigrum*, a climbing vine cultivated in the East Indies. It contains a crystalline alkaloid, *piperin*, an aromatic volatile oil, and a pungent resin.

PREPARATIONS

DOSE

Piperina.....	1-5 gr. (0.06-0.3 gm.)
Oleoresina Piperis, U. S. P.....	$\frac{1}{2}$ -2 min. (0.03-0.1 mil).

Therapeutics.—Pepper is used chiefly as a condiment. Owing to its carminative properties, the oleoresin is sometimes added to cathartic pills. Piperin was at one time considered to be of value in malarial fever, but for lack of satisfactory evidence of its efficacy its use in this affection has been entirely abandoned.

MENTHA PIPERITA, U. S. P.

(Peppermint)

Peppermint is the leaves and tops of *Mentha piperita*, a perennial herb growing in wet places throughout the temper-

ate zone. Its active principle is a greenish-yellow volatile oil, having a strong, characteristic odor and a pungent taste, followed by a sense of coolness when air is drawn into the mouth. When subjected to refrigeration or to fractional distillation it yields the stearopten, *menthol* (p. 175).

PREPARATIONS

DOSE

Oleum Menthæ Piperitæ, U. S. P.....	1-5 min. (0.06-0.3 mil)
Spiritus Menthæ Piperitæ, U. S. P. (10 per cent.)	10-30 min. (0.6-2.0 mils)
Aqua Menthæ Piperitæ, U. S. P.....	1-4 fl. dr. (4.0-15.0 mils).

The oil also enters into the official compound pills of rhubarb.

Therapeutics.—Peppermint has long been employed as a carminative for relieving *flatulence* and *colic*, especially in young children. It is particularly useful in covering the taste of unpalatable medicines. The oil, or better still menthol, is sometimes effective, when applied locally, in relieving the milder forms of *neuralgia* and *pruritus* (see p. 176).

MENTHA VIRIDIS, U. S. P.

(Spearmint)

Spearmint is the leaves and tops of *Mentha spicata*, a perennial herb growing wild in Europe and North America. Its active principle is a volatile oil.

PREPARATIONS

DOSE

Oleum Menthæ Viridis, U. S. P.....	1-5 min. (0.06-0.3 mil)
Spiritus Menthæ Viridis, U. S. P. (10 per cent.)	10-30 min. (0.6-2.0 mils)
Aqua Menthæ Viridis, U. S. P.....	1-4 fl. dr. (4.0-15.0 mils).

Spearmint is the therapeutic equivalent of peppermint.

CARDAMOMI SEMEN, U. S. P.

(Cardamom Seed)

Cardamom seed is the seed of *Elettaria repens*, a perennial herb cultivated in the mountainous regions of India. Its active principle is a volatile oil, of which it contains about 5 per cent.

PREPARATIONS

DOSE

Tinctura Cardamomi, U. S. P.....	1-2 fl. dr. (4.0-8.0 mils)
Tinctura Cardamomi Composita, U. S. P. (contains also cinnamon, caraway, cochineal, and glycerin).....	1-2 fl. dr. (4.0-8.0 mils)
Pulvis Aromaticus, U. S. P. (contains also ginger, cinnamon, and nutmeg).....	10-30 gr. (0.6-2.0 gm.).

Cardamom also enters into the compound extract of colocyth, compound tincture of gentian, and tincture of rhubarb.

Therapeutics.—It is used as an agreeable aromatic for disguising the taste of other drugs, and as an adjuvant to simple bitters in *flatulent dyspepsia*. When free acids are added to the compound tincture of cardamom they separate from the cochineal insoluble carminic acid, but this incompatibility is of no particular importance.

CARYOPHYLLUS, U. S. P.

(Cloves)

Cloves are the dried unexpanded flowers of *Eugenia aromatica*, an evergreen indigenous to the East Indian Islands, and cultivated to some extent in South America and Africa. They contain a yellow volatile oil of a characteristic odor and a pungent, spicy taste. The chief constituent of the oil is the stearopten, *eugenol*.

PREPARATIONS

DOSE

Oleum Caryophylli, U. S. P.....	1-5 min. (0.06-0.3 mil)
Eugenol, U. S. P.....	1-5 min. (0.06-0.3 mil).

They also enter into compound tincture of lavender and aromatic tincture of rhubarb.

Therapeutics.—Cloves are used as a counterirritant, local anesthetic, and carminative. They are one of the active ingredients of the *spice-poultice*, which consists of powdered cloves, ginger, and cinnamon, of each, one or two teaspoonfuls; flour, a tablespoonful; whiskey, sufficient to make a mass moist enough to spread on soft flannel. In this form they are a useful rubefacient for applying to the abdomen of children suffering from diarrhea. As a carminative, the oil is a useful addition to laxative pills, aiding materially in preventing *griping*. In *intestinal colic* brought on by chilling a drop or two of the oil in a teaspoonful of paregoric, repeated at short intervals, often gives speedy relief. The oil is also a popular remedy for *toothache*, being applied on a pledget of cotton to the cavity of the tooth.

MYRISTICA, U. S. P.

(Nutmeg)

Nutmeg is the seed of *Myristica fragrans*, an evergreen tree growing in the Molucca Islands and adjacent East India Islands. It contains a volatile oil, upon which its aromatic properties depend, and a fixed oil.

PREPARATION

DOSE

Oleum Myristicæ, U. S. P.....	1-5 min. (0.06-0.3 mil).
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Nutmeg also enters into aromatic powder, compound tincture of lavender, aromatic tincture of rhubarb, aromatic spirit of ammonia, and troches of sodium bicarbonate.

In large doses nutmeg acts as a narcotic poison, producing headache, vertigo, delirium, stupor, coma, and, finally, death from respiratory paralysis. Like cloves, it is employed as a carminative and a local anodyne.

ZINGIBER, U. S. P.

(Ginger)

The rhizome of *Zingiber officinale*, a perennial herb growing in tropical countries. It contains a volatile oil having the odor of ginger, and a viscid resinous principle having a hot, pungent taste.

PREPARATIONS	DOSE
Tinctura Zingiberis, U. S. P.	20-60 min. (1.2-4.0 mils)
Fluidextractum Zingiberis, U. S. P.	10-30 min. (0.6-2.0 mils)
Syrupus Zingiberis, U. S. P.	$\frac{1}{2}$ -4 fl. dr. (2.0-15.0 mils)
Oleoresina Zingiberis, U. S. P.	$\frac{1}{2}$ -2 min. (0.03-0.1 mil)

Ginger also enters into compound powder of rhubarb and aromatic powder.

Therapeutics.—It is employed as a carminative and as a flavoring agent.

CINNAMOMUM

(Cinnamon)

The United States Pharmacopœia recognizes two varieties of cinnamon: *Cinnamomum Saigonicum* (Saigon cinnamon), a species cultivated in the neighborhood of Saigon, the capital of French Cochin-China, and *Cinnamomum Zeylanicum* (Ceylon cinnamon). Cinnamon contains a volatile oil and a small amount of tannin. The oil consists chiefly of *cinnamic aldehyd*, which on exposure is oxidized into resin and *cinnamic acid*. The official oil (Oleum Cassiæ, U. S. P.) is distilled from *Cinnamomum Cassia*, or Chinese cinnamon.

PREPARATIONS	DOSE
Oleum Cassiæ, U. S. P.	1-5 min. (0.06-0.3 mil)
Spiritus Cinnamomi, U. S. P. (10 per cent. of oil)	10-30 min. (0.6-2.0 mils)
Tinctura Cinnamomi, U. S. P.	$\frac{1}{2}$ -2 fl. dr. (2.0-8.0 mils)
Aqua Cinnamomi, U. S. P.	$\frac{1}{2}$ -1 fl. oz. (15.0-30.0 mils).

Cinnamon also enters into aromatic fluidextract, infusion of digitalis, compound tincture of cardamom, compound tincture

of lavender, compound tincture of gambir, aromatic fluidextract of cascara sagrada, and aromatic powder.

Therapeutics.—Cinnamon possesses carminative and feebly astringent properties. The oil is an active antiseptic. Cinnamon water is an agreeable vehicle for *diarrhea* mixtures. The oil has been used to some extent as an antiseptic in surgical dressings. Favorable results have been reported from the use of cinnamon in *influenza*.

Cinnamic acid and its sodium salt have been highly extolled by Landerer, Heusser, and others in the treatment of *tuberculosis*. It is claimed that intravenous injections of sodium cinnamate ($\frac{1}{8}$ gr.—0.008 gm.—every forty-eight hours, gradually increased to $\frac{1}{3}$ gr. 0.02 gm.) induce a marked hyperleukocytosis and favor the formation of cicatricial tissue around the tuberculous area. A careful review of the reported cases, however, does not warrant the belief that this method of treatment is any more effective than other methods that are much less painful.

OLEUM CAJUPUTI, U. S. P.

(Oil of Cajuput)

Oil of cajuput is a thin, bluish-green, volatile oil distilled from the leaves of *Melaleuca Leucadendron*, a small tree growing in the East India Islands. It has a camphoraceous odor and an aromatic, bitter taste. The dose is from 2 to 10 minims (0.12–0.6 mil) in emulsion, in capsules, or on sugar.

Therapeutics.—Cajuput oil is one of the most efficient of the carminatives. It is an excellent adjuvant to other remedies in the *flatulent dyspepsia* of the aged. Combined with opium it is undoubtedly useful in *diarrhea* with choleraic symptoms. It has been used also as a rubefacient in *myalgia* and as a parasiticide in *ringworm*.

ANISUM, U. S. P.

(Anise)

Anise is the fruit of *Pimpinella Anisum*, a small plant cultivated in Southern Europe and North America. It contains a volatile oil having the characteristic odor of anise and a sweetish, aromatic taste.

PREPARATIONS	DOSE
Oleum Anisi, U. S. P.	2–5 min. (0.12–0.3 mil)
Aqua Anisi, U. S. P.	2–8 fl. dr. (8.0–30.0 mls)
Spiritus Anisi, U. S. P. (10 per cent. of oil).....	1–2 fl. dr. (4.0–8.0 mls).

Anise also enters into camphorated tincture of opium, compound spirit of orange, aromatic elixir, compound syrup of sarsaparilla and aromatic fluidextract of cascara sagrada.

Therapeutics.—Although anise is an effective carminative, it is used chiefly as a flavoring agent.

PIMENTA

(Allspice)

Allspice is the nearly ripe fruit of *Pimenta officinalis*, an evergreen tree growing in the West Indies and South America. It contains a volatile oil, the active constituent of which is *eugenol*.

PREPARATION	DOSE
Oleum Pimentæ, U. S. P.....	1-5 min. (0.06-0.3 mil).

SASSAFRAS

Sassafras is the bark of *Sassafras variifolium*, a shrub or tree growing in Eastern North America. It contains a fragrant, aromatic, volatile oil and a moderate amount of tannin (6 per cent.).

PREPARATION	DOSE
Oleum Sassafras, U. S. P.....	1-5 min. (0.06-0.3 mil).

Sassafras also enters into compound fluid extract of sarsaparilla, compound syrup of sarsaparilla, and troches of cubeb.

CARUM, U. S. P.

(Caraway Seed)

Caraway is the dried fruit of *Carum Carvi*, an herb indigenous to Asia, and cultivated in Europe and North America. Its active ingredient is a volatile oil.

PREPARATION	DOSE
Oleum Cari, U. S. P.....	1-5 min. (0.06-0.3 mil).

Caraway also enters into compound tincture of cardamom and compound spirit of juniper.

FÆNICULUM, U. S. P.

(Fennel)

Fennel is the fruit of *Fœniculum vulgare*, grown chiefly in Southern Europe. It contains an aromatic volatile oil.

PREPARATIONS	DOSE
Oleum Fœniculi, U. S. P.....	1-5 min. (0.06-0.3 mil)
Aqua Fœniculi, U. S. P.....	1-8 fl. dr. (4.0-30.0 mls).

Fennel also enters into compound licorice powder, compound spirit of juniper, and compound infusion of senna.

CORIANDRUM, U. S. P.

(Coriander)

Coriander is the dried fruit of *Coriandrum sativum*, an herb grown in all parts of Europe and the United States. It contains a volatile oil.

PREPARATION

DOSE

Oleum Coriandri, U. S. P. 1-5 min. (0.06-0.3 mil).

Coriander also enters into confection of senna, syrup of senna, aromatic fluidextract of cascara sagrada, and compound spirit of orange.

OTHER CARMINATIVES

The carminative properties of *asafetida*, *ether*, *compound spirit of ether*, *chloroform*, and *oil of turpentine* are discussed elsewhere in this volume.

CATHARTICS

Cathartics are drugs that are used to cause evacuation of the bowels. They may act by irritating the intestines or by augmenting the bulk of the feces. In the first instance intestinal peristalsis is increased directly, and in the second instance it is increased indirectly by distention of the bowel. *Vegetable cathartics* (castor oil, rhubarb, aloes, jalap, podophyllum, etc.), *calomel*, and *phenolphthalein* act through their irritant properties. These drugs also render the stools more or less watery; but this effect is to be ascribed to the rapid evacuation of the intestinal contents and the escape of much liquid that would otherwise be reabsorbed, or, in case the action of the drug has been more or less violent, to the development of a true inflammatory process with serous exudation.

Saline cathartics do not irritate the bowel unless given in very large doses. On the other hand, they retard the absorption of liquids (if in isotonic or hypotonic solution) and withdraw water from the blood (if in hypertonic solution), and thus, by distending the bowel, stimulate peristaltic movements. Only salts that are difficult of absorption, such as the sulphates, phosphates, and tartrates, have a purgative effect. Magnesium sulphate is especially active in this respect, as neither its basic nor its acid ion is readily absorbed. Nitrates, chlorides, acetates, and other rapidly

absorbed salts induce diuresis rather than purgation because they draw water from the tissues into the blood, and so increase the capillary pressure in the kidneys.

Agar, liquid petrolatum and olive oil promote defecation by giving bulk and soft consistency to the stools.

It was formerly believed that certain cathartics, such as calomel and sodium phosphate, stimulate the liver and increase the secretion of bile, and, in consequence, these drugs were known as *cholagogues* or *cholagogue cathartics*. No reliable evidence, however, was adduced in support of this assumption. It is true that the group of symptoms to which the term "biliousness" is applied often disappears as by magic after the administration of a full dose of calomel, but there is no proof that these symptoms are due to inactivity of the liver; on the contrary, there is much to support the view that they are due solely to some derangement of the stomach and intestines. Nor can the dark green color of the stools that is observed after the administration of certain cathartics be claimed as an evidence of increased biliary secretion, for it is doubtless due, in large part, to the rapid flow of bile into the lower bowel and its escape from decomposition and reabsorption. Rutherford ligated the common bile-duct, inserted a cannula into it, and then noted the effect that the injection of certain drugs into the duodenum had upon the flow of bile. From his experiments he concluded that the following drugs increase the secretion of bile:

Podophyllin	Jalap
Aloes	Sodium sulphate
Rhubarb	Sodium phosphate
Iridin	Rochelle salt
Colocynth	Euonymin
Ipecacuanha.	

Unfortunately, Rutherford's experiments were too few in number and his results too often contradictory to justify his conclusions, and, moreover, recent investigations, especially those of Stadelmann and Pfaff, have failed completely to confirm the facts embodied in Rutherford's report. The only body known to have a decided cholagogue action is bile itself, although salicylic acid and its salts also promote the biliary secretion to a slight extent.

The colicky pains often induced by cathartics are probably due chiefly to a stimulating effect which extends beyond the ganglia of Auerbach's plexus and involves the vagus nerves, thereby exciting spasmodic contractions of the bowel or cramps. That they may be caused also by scybala interrupting the normal

peristaltic movements and throwing the muscular fibers into spasm is evident from the experiments of Cash, who found that the slightest weight sufficed to check the onward movement of the substance in the intestine and to set up contractions of a painful character.

Classification.—Cathartics have been variously classified according to the intensity of their action and the character of the stools that they produce. Since the effect of any cathartic is dependent to a great extent upon the dose, the time of administration, the susceptibility of the patient, and the state of the bowel, it is evident that a classification based upon the degree of activity must necessarily be an imperfect one; nevertheless, if we recognize its limitations, such a classification is a convenient one for clinical purposes. Cathartics, therefore, may be divided into laxatives, purgatives, drastics, and hydragogues.

Laxatives are the least irritating of all the cathartics, and ordinarily produce stools that are nearly normal in appearance and consistence. Many articles of food, such as molasses, bran bread, figs, prunes, apples, etc., serve as laxatives. The most important drugs belonging to this class are:

Manna	Euonymus
Tamarind	Iris
Cascara sagrada	Leptandra
Frangula	Ox-gall
Magnesia	Agar
Sulphur	Liquid petrolatum.

Purgatives are more powerful than laxatives, and usually produce one or more copious stools of a semiliquid consistence. The difference between the action of a laxative and that of a purgative is mainly one of degree; laxatives in large doses act as purgatives, and the latter in small doses act as laxatives. The most important purgatives are:

Aloes	Castor oil
Rhubarb	Calomel
Senna	Blue mass.

Drastics have a violent action and in overdoses produce the symptoms of acute enteritis. The most important are:

Croton oil	Podophyllum
Colocynth	Jalap
Gamboge	Elaterium
Scammony root	Bryonia.

Hydragogues produce large watery stools and give rise to but slight irritation. The principal ones are:

Magnesium sulphate	Potassium and sodium tartrate
Sodium sulphate	Sodium phosphate
Magnesium citrate.	

Some of the drastics, especially jalap, elaterium, and bryonia, in appropriate doses, are effective hydragogues.

Indications.—*To Relieve Constipation.*—In *simple acute constipation* the prompt administration of a cathartic or the employment of an enema is nearly always advisable. In *chronic constipation* recourse should first be had to dietetic and hygienic measures, but, these failing, a laxative should be prescribed. As a rule, the use of laxatives in these cases, even when habitual, is less baneful than the persistent constipation. Indeed, mild vegetable cathartics are often taken for indefinite periods without producing harmful effects. Brodie speaks of a man, eighty-six years of age, who for threescore years took an aloetic pill every night.

To Remove Irritants from the Bowel.—In the beginning of *acute diarrhoea* it is nearly always advisable to administer a dose of castor oil, calomel, or Epsom salts, to rid the bowel of undigested material, putrefactive products, and microorganisms. In *poisoning*, if the irritant has escaped from the stomach into the bowel, a purgative should take the place of an emetic.

To Promote Absorption.—Hydragogue cathartics, especially the salines, are often useful in *cardiac* and *renal dropsy*. They not only remove directly from the body a certain amount of fluid, but, by depleting the blood, promote the reabsorption of the lymph that has accumulated in the tissues.

In *serous effusions* of an inflammatory character, such as are met with in *pleurisy* and *pericarditis*, cathartics are rarely serviceable.

Certain drugs, such as digitalis and quinin, may prove ineffective until the bowel has been unloaded and the portal system depleted by the administration of a brisk cathartic.

To Remove Excrementitious Substances from the Blood.—In *uremia* and *puerperal eclampsia* the administration of cathartics is a measure of the greatest value in securing the elimination of noxious material.

To Relieve Cerebral Congestion.—In *acute cerebral congestion* cathartics serve a useful purpose, since, by inviting blood to the bowel, they tend to deplete the brain. In *cerebral hemorrhage*, also, they may do good by preventing further extravasation.

Contraindications.—Acute intestinal obstruction, acute appendicitis and threatened intestinal hemorrhage are absolute contraindications. Strong cathartics should be avoided in inflammation of the gastrointestinal tract, pregnancy and all conditions in which there is pronounced systemic weakness.

Administration.—Cathartics are most commonly administered by the mouth. The salines are given in solution; the vegetable preparations, most conveniently in the form of pills. In chronic constipation a combination of several drugs usually gives rise to less pain and is more effective than a single drug. A small amount of the extract of belladonna or a drop of one of the aromatic oils is frequently employed as an adjuvant to prevent griping. If atony of the bowel is pronounced, extract of nux vomica or of physostigma may be added to the pill to enhance its stimulating effect. The time of administration is a factor to be considered in prescribing any cathartic. Pills of the vegetable cathartics are likely to cause less inconvenience if administered after the evening meal or on going to bed. Salines or saline mineral waters act more promptly and powerfully when given before breakfast.

Very often an *enema* is the most satisfactory means of unloading the bowel. A metal or hard rubber syringe with a piston or one made entirely of soft rubber may be employed for the purpose. The syringe should be filled with the fluid; all the air should be expelled from it before the nozzle is inserted. The patient should lie near the edge of the bed, on the left side, with the knees drawn up. A towel should be held against the anus on withdrawing the nozzle, so that the fluid may be retained in the bowel for several minutes. An enema may act by distending the bowel (mechanically), by softening the intestinal contents, or by directly irritating the intestinal walls.

A simple enema is one composed of cool or tepid water or of soap and water. For an infant, 1 or 2 ounces (30.0–60.0 mls) may be employed; for a child, from 4 to 8 ounces (120.0–240.0 mls); and for an adult, from 1 to 2 pints (0.5–1.0 L.). The injection may be made more powerful by adding, in the case of an adult, 1 ounce (30.0 mls) of castor oil, $\frac{1}{2}$ ounce (15.0 mls) of molasses, or from 1 to 2 drams (4.0–8.0 mls) of oil of turpentine. The following enema, official in the British Pharmacopœia, is very useful:

Magnesium sulphate.....	1 ounce (30.0 mls)
Olive oil.....	1 ounce (30.0 mls)
Mucilage of starch.....	15 ounces (450.0 mls).

A small enema of glycerin (1–2 drams—4.0–8.0 mls) is generally efficacious. In cases of fecal impaction an enema of

warm salad or linseed oil (6-8 ounces—180.0-240.0 mls) or an infusion of ox-gall often proves serviceable. In some cases of chronic indigestion with constipation flushing out the lower bowel with from 6 to 8 pints (3.0-4.0 L.) of tepid water, two or three times a week, by means of a soft-rubber tube passed well up into the sigmoid flexure, is followed by excellent results.

It is well to remember that bulky enemata containing hard soap are occasionally followed, after the lapse of a few hours, by a scarlatiniform, measly, or urticarial rash.

The introduction into the rectum of *suppositories* made of yellow scap, glycerin, or gluten is another means frequently employed to unload the bowel.

It has been shown that certain drugs—aloin, colocynthin, and cathartic acid—will produce catharsis when given hypodermically. The irritation caused by the injections of these substances, however, is so severe as to forbid the employment of this method of administration except under very unusual circumstances.

MANNA, U. S. P.

Manna is the dried saccharine exudation of *Fraxinus Ornus*, a small tree indigenous to Sicily and other Mediterranean islands. It occurs in the form of yellowish-white or brownish-white three-edged pieces or fragments, having a crystalline structure, a honey-like odor, and a sweetish, faintly acrid taste. Its chief constituent is *mannite* (50-80 per cent.), a sweet crystalline principle soluble in water. In doses of from $\frac{1}{2}$ to 2 ounces (15.0-60.0 gm.) manna acts as a mild laxative. It is usually given in combination with other cathartics.

PREPARATION

DOSE

Infusum Sennæ Compositum, U. S. P. (Black Draft)..... 1-4 fl. oz. (30.0-120.0 mls).

TAMARINDUS

(Tamarind)

Tamarind is the preserved pulp of the fruit of *Tamarindus indicus*, a large tree indigenous to Africa, and cultivated in the West Indies. It is a gentle laxative, about equal in power to the fig and prune. Its aperient properties are due chiefly to the potassium salts of tartaric, citric, malic, and acetic acids, of which it contains from 8 to 12 per cent. The dose is from 1 to 8 drams (4.0-30.0 gm.).

AGAR, U. S. P.

(Agar-agar)

Agar-agar is the dried mucilaginous substance extracted from various species of seaweed growing along the coast of Asia. It consists chiefly of a hemicellulose, which has the property of absorbing water to form a jelly. It is not acted upon by the digestive enzymes and it is not absorbed from the alimentary canal, but as it absorbs and retains water it gives bulk and soft consistency to the feces, and thus acts mechanically as a mild laxative.

Agar is sometimes useful in *habitual constipation*, especially if the stools are abnormally dry. It may be given in doses of 2 to 4 teaspoonfuls, once or twice a day, either dry or mixed with a breakfast cereal or cooked fruits. It may also be used in hard biscuits. The effect is often delayed for several days. In many cases it proves unsatisfactory unless small doses of some other laxative, such as cascara sagrada or phenolphthalein, are used in addition.

PETROLATUM LIQUIDUM, U. S. P.

(Liquid Petrolatum, Liquid Paraffin, Mineral Oil)

Liquid petrolatum is a colorless, odorless and tasteless mixture of liquid hydrocarbons. The dose is from $\frac{1}{2}$ to 1 ounce (15.0–30.0 mls), with cold water or orangeade at night or two or three times a day, between meals, that is when the stomach is empty.

Liquid petrolatum is often useful when the stools are dry and hard, or the constipation is the result of partial obstruction, is accompanied by mucous colitis, or is of the spastic type, occurring in association with peritoneal adhesions, chronic appendicitis, chronic cholecystitis, ovarian disease, anal fissure etc. In simple atonic constipation it is much less efficient. It is not rarely necessary to add a small amount of cascara to secure the best results. Drawbacks are interference with the absorption of food products, protection of the bowel from the action of natural stimuli through the emollient properties of the oil, the tendency of the oil to cause nausea and eructations, and also, in some individuals, to “dribble” from the anus. Heavy viscid oils are usually preferred, but, according to Bastedo, the physical properties of the oil do not influence the clinical effects.

CASCARA SAGRADA, U. S. P.

(Rhamnus Purshiana)

Cascara sagrada is the dried bark of *Rhamnus Purshiana*, a small tree growing in Northern California, Oregon, and Washing-

ton. It is allied to *Rhamnus Frangula* (buckthorn) and to *Rhamnus cathartica* (buckthorn). It contains *emodin* and other anthracen derivatives,* and so is allied chemically to frangula, rhubarb, aloes, and senna.

PREPARATIONS

DOSE

Fluidextractum Cascaræ Sagradæ, U. S. P.	10-30 min. (0.6-2.0 mls)
Fluidextractum Cascaræ Sagradæ Aromaticum, U. S. P.	10-30 min. (0.6-2.0 mls)
Extractum Cascaræ Sagradæ, U. S. P.	2-5 gr. (0.13-0.3 gm.).

Therapeutics.—Cascara sagrada is used exclusively as a tonic laxative, and in *habitual constipation* due to torpor of the bowel it is a most reliable remedy. It possesses an advantage over many cathartics in not readily losing its effect when frequently taken; indeed, in many cases the dose may be diminished gradually and still give satisfactory results.

In most cases a single dose at bedtime will afford relief, but sometimes small doses (10 drops of the fluidextract) after each meal are more effective. On account of its unpleasant bitter taste the fluidextract is best given in some aromatic syrup or cordial, as in the following formula:

R. Fluidextracti cascaræ sagradæ
Fluidextracti sarsaparillæ compositi
Glycerini āā f 3i (30.0 mls).—M.
Sig.—A teaspoonful to a dessertspoonful.

FRANGULA, U. S. P.

(Buckthorn)

Frangula is the bark of *Rhamnus Frangula*, a shrub growing in Europe and Northern Asia. Its activity depends upon the anthracen body, *emodin*.

PREPARATION

DOSE

Fluidextractum Frangulæ, U. S. P. . . ½-1 fl. dr. (2.0-4.0 mls).

Frangula has an action similar to that of cascara sagrada, but more powerful.

* These bodies are substitution products of anthraquinon ($C_{14}H_8O_2$). Among them are *emodin*, *cathartinic acid*, and *chrysophanic acid*. They act mainly on the colon and rectum. Being somewhat readily absorbed in the free state, they are less effective as cathartics than the crude drugs and the galenical preparations containing them. Several synthetic anthracen compounds have been put upon the market as substitutes for the crude drugs. Among these are purgatin, exodin, and purgen (phenolphthalein).

ALOE, U. S. P.

(Aloes)

Aloes is the inspissated juice of the leaves of several species of the genus *Aloe*, a familiar example of which is the American century plant. It contains a crystalline body *aloin*, a resin, and a trace of volatile oil. Aloin is a mixture of anthracen bodies similar to those contained in cascara sagrada, rhubarb and senna. It is less efficient than the crude drug and more irritant. The dose of aloes is from 1 to 5 grains (0.065–0.3 gm.).

PREPARATIONS	Dose
Aloinum, U. S. P.	$\frac{1}{8}$ – $\frac{1}{2}$ gr. (0.008–0.03 gm.)
Pilulæ Aloes, U. S. P. (about 2 gr.–0.13 gm.)...	1–2 pills
Pilulæ Rhei Compositæ, U. S. P. (aloes with rhubarb and myrrh).....	1–3 pills
Tinctura Aloes, U. S. P.	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls)
Pilulæ Aloini, Belladonnæ et Strychninæ (each contains aloin, $\frac{1}{5}$ gr.–0.013 gm.; strychnin, $\frac{1}{20}$ gr.–0.0005 gm.; and extract of bella- donna, $\frac{1}{8}$ gr.–0.008 gm.).....	1–3 pills

Aloes also enters into compound extract of colocynth and compound tincture of benzoin.

Pharmacologic Action and Therapeutics.—Aloes is a slowly acting but brisk purgative. A dose of 2 or 3 grains ordinarily produces one or two copious, dark brown stools in the course of eight or ten hours. The evacuation is generally attended with more or less griping pain. Large doses congest the pelvic viscera and irritate the rectum. It has been shown that a part of that which is ingested escapes from the body in the urine, and, in the case of nursing women, in the milk. Aloes also causes catharsis when introduced into the system through channels other than the mouth, such as the skin and the rectum. When injected into the bowel, however, it is active only when combined with a solvent, such as ox-gall or glycerin. Aloes is rarely used singly as a cathartic, but in *simple, persistent constipation* it is very efficacious in combination with other remedies, particularly with nux vomica, belladonna, ipecac, rhubarb, or podophyllum. *Chlorosis* with constipation often yields to pills of aloes and iron. Contrary to what was formerly believed, the use of aloes is not contraindicated by the existence of hemorrhoids unless inflammation has developed; indeed, the drug often benefits *indolent piles* by overcoming the sluggishness of the bowel that led to their development. Since it congests the pelvic organs, aloes is sometimes serviceable as an emmenagogue in *amenorrhea* associated with troublesome

constipation, and that is not dependent upon inflammation of the uterus or adnexa.

When dysentery, cystitis, or inflammation of any pelvic organ is present aloes should be avoided. On account of the possibility of its causing abortion it is best not to use it during pregnancy.

Aloes is usually administered in the form of pills. The tincture, on account of its disagreeable taste, is rarely employed.

RHEUM, U. S. P.

(Rhubarb)

Rhubarb is the root of *Rheum officinale* and other species of *Rheum*, a perennial herb resembling garden rhubarb, but of larger growth, and a native of China, Thibet, and other Asiatic countries. It contains a number of anthracen bodies (*emodin*, *cathartinic*, and *chrysophanic acid*) and a considerable quantity of *tannin*. Chrysophanic acid has not the purgative action of the other anthracen bodies, owing to its rapid absorption. The dose of rhubarb is from 5 to 30 grains (0.3–2.0 gm.).

PREPARATIONS	DOSE
Tinctura Rhei, U. S. P. (20 per cent., with cardamom).....	1–2 fl. dr. (4.0–8.0 mls)
Tinctura Rhei Aromatica, U. S. P. (20 per cent., with aromatics).....	½–1 fl. dr. (2.0 4.0 mls)
Fluidextractum Rhei, U. S. P.	10–30 min. (0.6–2.0 mls)
Extractum Rhei, U. S. P.	2–5 gr. (0.13–0.3 gm.)
Syrupus Rhei, U. S. P. (10 per cent. of fluid extract).....	1–4 fl. dr. (4.0–15.0 mls)
Syrupus Rhei Aromaticus, U. S. P. (spiced syrup of rhubarb: 15 per cent. of aromatic tincture).....	1–4 fl. dr. (4.0–15.0 mls)
Pulvis Rhei Compositus, U. S. P. (Gregory's powder: rhubarb, 25; magnesia, 65; ginger, 10).....	20–60 gr. (1.3–4.0 gm.)
Pilulæ Rhei Compositæ, U. S. P. (rhubarb, 2 gr.—0.13 gm.; aloes, 1½ gr.—0.1 gm.; myrrh; and oil of peppermint).....	1–3 pills.

Pharmacologic Action and Therapeutics.—In appropriate doses rhubarb acts as a purgative and stomachic. It affects the bowel more promptly than aloes, a full dose of from 20 to 30 grains (1.3–2.0 gm.) usually producing evacuation in from four to eight hours. On account of the tannin that it contains it frequently causes constipation as a secondary effect. Doses of from 1 to 3 grains (0.065–0.2 gm.) often exert no cathartic influence, but act upon the stomach as a tonic and mild astringent. It is eliminated in the various secretions—urine, milk, and sweat—and imparts to them a yellowish color.

Rhubarb is an excellent remedy for removing irritant material from the bowel in the beginning of *acute diarrhea*. In the *dyspeptic diarrhea of childhood* the withdrawal of all food for several hours and the administration of a few doses of the aromatic syrup with magnesia often affords prompt relief:

℞. Magnesii oxidi..... gr. xl (2.6 gm.)
 Syrupi rhei aromatici..... f ʒ vj (22.5 mls.)
 Aquæ menthæ piperitæ... q. s. ad f ʒ j (30.0 mls).—M.
 SIG.—A teaspoonful repeated once or twice for a child two years old.

Rhubarb alone is not a suitable remedy for *chronic constipation*, but benefit is often derived from a combination of small doses with other cathartics. *Mild attacks of indigestion*, the result of intemperance in eating, frequently yield to the union of rhubarb with an antacid:

℞. Pulveris nucis vomicæ..... gr. xii (0.8 gm.)
 Pulveris rhei..... gr. xxiv (1.5 gm.)
 Sodii bicarbonatis..... ʒ j (4.0 gm.).—M.
 Fiant chartulæ No. xii.
 SIG.—One before meals.

SENNA, U. S. P.

Senna is the leaflets of *Cassia acutifolia* and of *Cassia angustifolia*, small shrubs growing respectively in Africa and India. It contains a number of anthracen bodies, chief of which is *carthartinic acid*. The dose is from 1 to 2 drams (4.0–8.0 gm.).

PREPARATIONS	Dose
Fluidextractum Sennæ, U. S. P.....	½–1 fl. dr. (2.0–4.0 mls)
Syrupus Sennæ, U. S. P. (25 per cent.).....	1–2 fl. dr. (4.0–8.0 mls)
Infusum Sennæ Compositum, U. S. P. (Black Draft: senna, 6; fennel, 2; manna, 12; Epsom salts, 12).....	1–4 fl. oz. (30.0–120.0 mls)
Pulvis Glycyrrhizæ Compositus, U. S. P. (18 per cent. of senna, with licorice, sulphur, sugar, and fennel oil).....	½–2 dr. (2.0–8.0 gm.).

Senna (1.5 per cent. of the fluid extract) also enters into compound syrup of sarsaparilla.

Pharmacologic Action and Therapeutics.—Senna is an energetic purgative, acting chiefly on the large intestine. A full dose produces in from four to six hours one or two yellowish, loose, or even watery, stools, the evacuation being attended with considerable griping and flatulence. Its action is more irritating than that of rhubarb, and more prompt and powerful than that of aloes. Very large doses cause nausea, vomiting, violent purging, and depression. Cathartinic acid also acts

when injected subcutaneously. Like rhubarb, senna imparts to the urine a deep yellow or red color, the pigmentation being due to the presence of chrysophanic acid. Senna is a safe and reliable purgative for unloading the bowel in *simple acute constipation*.

PHENOLPHTHALEINUM, U. S. P.

(Phenolphthalein, $(C_6H_4OH)_2CO.C_6H_4CO$)

Phenolphthalein is a dibasic phenol derivative, prepared by the interaction of phenol and phthalic anhydride. It is a white, odorless and tasteless crystalline powder, soluble in about 13 parts of alcohol and almost insoluble in water. The dose is 1 to 3 grains (0.065–0.2 gm.) in pill, tablet, capsule, or powder.

Pharmacologic Action and Therapeutics.—Phenolphthalein is a mild and agreeable laxative, yielding satisfactory results in many cases of *habitual constipation*. It is excreted almost entirely in the feces, although traces sometimes appear in the urine. In the doses indicated, the drug appears to be safe. Even very large doses have rarely caused more than severe intestinal irritation. However, one observer (Hydrick) found albuminuria regularly after doses of 1 to 2 grains (0.065–0.13 gm.), and a number of observers have reported a somewhat persistent eruption of an erythematous character as a result of the long continued use of the drug.

Phenolphthalein may often be combined advantageously with other laxatives, such as cascara sagrada, rhubarb, and podophyllum. It enters into a large number of proprietary cathartic medicines.

EUONYMUS

(Wahoo)

Euonymus is the dried bark of the root of *Euonymus atropurpureus*, growing in eastern North America. It contains an amorphous glucosid, *euonymin*, which affects the circulation somewhat like digitalis.

PREPARATION

DOSE

Extractum Euonymi..... 1–5 gr. (0.06–0.3 gm.).

The cathartic action of euonymus resembles that of podophyllum, although it is less powerful. The drug has been credited with cholagogue as well as laxative properties, but there is no evidence to support this assumption.

IRIS

(Blue Flag)

Blue flag is the rhizome and roots of *Iris versicolor*, a perennial herb growing in the swampy places of North America.

PREPARATION

DOSE

Extractum Iridis. 1-5 gr. (0.06-0.3 gm.).

The action of iris resembles that of podophyllum, although it is milder. At one time held in high esteem, the drug has at present fallen into disuse.

LEPTANDRA

(Culver's Root)

Leptandra is the rhizome and roots of *Veronica virginica*, a perennial herb growing in the eastern portion of the United States. It contains an amorphous bitter principle.

PREPARATIONS

DOSE

Fluidextractum Leptandræ. 10-30 min. (0.6-2.0 mls)

Extractum Leptandræ. 1-5 gr. (0.06-0.3 gm.).

In the fresh state leptandra is an active gastrointestinal irritant. Preparations made of the dried roots usually have a laxative or purgative effect, according to the dose, but they are somewhat uncertain in their action. Leptandra has been largely superseded by more reliable remedies.

OLEUM RICINI, U. S. P.

(Castor Oil)

Castor oil is a fixed oil expressed from the seed of *Ricinus communis*, a plant indigenous to India, but extensively cultivated in other countries having a warm or temperate climate. It is a pale-yellowish, viscid oil, having a faint odor and a slightly acrid, offensive taste. It is freely soluble in alcohol. It is composed chiefly of *ricinolein*, the triglycerid of ricinoleic acid, which is the purgative principle. The seeds themselves are never used for medicinal purposes. They contain *ricin*, an intensely poisonous protein, which, when injected into the blood of an animal, causes, after the lapse of several days, anorexia, vomiting, diarrhea, and profound prostration. In fatal poisoning the chief postmortem lesions are extensive ecchymoses of the mucous and serous membranes, tumefaction of the abdominal lymph-nodes, and numerous areas of necrosis in the various organs. The dose of castor oil for an infant is from 1 to 2 drams (4.0-8.0 mls); for an adult, $\frac{1}{2}$ to 1 ounce (15.0-30.0 mls).

Pharmacologic Action and Therapeutics.—Castor oil is a mild purgative, unloading the bowels thoroughly in from three to six hours, without causing much colic or flatulence. While its fate in the body has not been definitely determined, it is probable that it escapes from the stomach unchanged, and that in the presence of the intestinal juices saponification occurs with the liberation of ricinoleic acid, which is subsequently converted into ricinoleates. The latter induce catharsis by stimulating the muscular coat of the bowel, especially that of the small intestine, and are probably absorbed to some extent, since the oil is known to impart its purgative properties to the milk when given to nursing women.

Castor oil is not a suitable remedy for habitual constipation, but on account of its mild and speedy action it is perhaps the best remedy we possess to remove irritant material from the bowel in the beginning of *acute inflammatory diarrhea*. It is also an excellent laxative for use during *pregnancy* or *labor*.

When it is desirable to add an oil to a lotion intended for the scalp, castor oil is usually selected on account of its solubility in alcohol.

Many substances have been suggested to disguise the disagreeable taste of castor oil, which is the main objection to its employment; those in common use are the oils of peppermint, gaultheria, and cinnamon. Wood speaks favorably of a combination of equal parts of glycerin and castor oil flavored with a drop or two of one of the above-named oils. It is often given in the froth of porter, beer, or soda-water or on black coffee. It may be prescribed in emulsion, but in this form it is bulky and not so effective. A good method of administering it is in flexible capsules containing a dram (30.0 mils) or more.

OLEUM TIGLII, U. S. P.

(Croton Oil)

Croton oil is a fixed oil expressed from the seeds of *Croton Tiglium*, a small tree, indigenous to China, but extensively cultivated in India and the Philippine Islands. It is a yellowish, viscid oil, having a faint odor and an acrid, burning taste. In addition to several inactive fatty acids it contains *crotonoleic acid*, which is present both as a free acid and as a glycerid. The dose of the oil is from $\frac{1}{2}$ to 2 minims (0.03–0.12 mil).

Pharmacologic Action and Therapeutics.—When applied to the skin, croton oil causes redness and burning, followed by a copious eruption of pustules and even by sloughing. When taken internally, it acts as a violent drastic cathartic, causing in from one to two hours several copious movements, which are

partly formed and partly watery. The evacuations are usually attended with considerable pain, and not infrequently with nausea. Large doses produce all the symptoms of a severe gastroenteritis. As croton oil contains a certain amount of free crotonoleic acid, it causes, when swallowed without a demulcent, a burning sensation in the fauces and stomach, but its maximum irritant effect is not manifested until it reaches the intestine, where the bulk of the acid is liberated from the oil by saponification.

On account of the ease with which it can be administered croton oil is a well-adapted cathartic for cases in which deglutition is seriously affected. Its prompt irritant action on the bowel makes it also a useful revulsant in cases of cerebral congestion. Thus, it may be given with advantage in *uremia* and *cerebral hemorrhage*.

It is also useful in very *obstinate constipation*, such as occurs in chronic lead-poisoning. Its use is contraindicated whenever there is inflammation of the gastrointestinal tract.

The drug is best administered in olive oil or in a pill with bread-crumbs as an excipient.

Croton oil is sometimes used externally as a counterirritant. It is rarely applied to the skin in the pure state, a mixture with from 3 to 6 parts of some indifferent oil usually being preferred. A liniment is official in the British Pharmacopœia that contains 12 per cent. of the oil in equal volumes of oil of cajuput and alcohol. This liniment may be applied to the chest in *chronic bronchitis* or *fibrinous pleurisy*.

A mixture of croton oil (1 part) and tincture of iodine (4 parts) employed as a pigment often acts well in *neuritis*.

COLOCYNTHIS, U. S. P.

(Colocynth, Bitter Apple)

Colocynth is the fruit of *Citrullus Colocynthis* deprived of its rind. The plant grows in arid places in Asia, Africa, and Southern Europe. It contains an alkaloid and a resin.

PREPARATIONS

DOSE

Extractum Colocynthis, U. S. P.	½–2 gr. (0.03–0.13 gm.)
Extractum Colocynthis Compositum, U. S. P. (extract of colocynth, 16; aloes, 50; resin of scammony, 14; cardamom, 6; soap, 14)	2–10 gr. (0.13–0.6 gm.)
Pilulæ Catharticæ Compositæ, U. S. P. (each pill contains about 1¼ gr.—0.08 gm.—of com- pound extract of colocynth; 1 gr.—0.06 gm.— of calomel, ⅓ gr.—0.02 gm.—of resin of jalap; ¼ gr.—0.015 gm.—of gamboge)	1–3 pills.

Pharmacologic Action and Therapeutics.—Colocynth is a powerful drastic cathartic, producing in full doses copious watery stools, which are often accompanied by griping. Very large doses excite intense inflammation of the whole alimentary tract, which may prove fatal. The drug is too irritant to be used alone. At the present time it is prescribed in combination with other remedies only in *obstinate chronic constipation*. It is not a suitable cathartic for habitual use, but it may be employed now and then to secure a thorough evacuation of the bowels.

CAMBOGIA, U. S. P.

(Gamboge)

Gamboge is a gum-resin from *Garcinia Hanburii*, a laurel-like tree growing in the East Indies. It owes its activity to *garanolic acids*. The dose is from $\frac{1}{2}$ to 3 grains (0.03–0.2 gm.)

PREPARATION

DOSE

Pilulæ Catharticæ Compositæ, U. S. P. (about $\frac{1}{4}$ gr.—0.015 gm.
—in each pill)..... 1–3 pills.

Pharmacologic Action and Therapeutics.—Gamboge is an extremely irritating drastic cathartic, fully capable in large doses of causing fatal gastro-enteritis. It is never used alone, but in combination with less powerful cathartics it is sometimes employed in *obstinate chronic constipation*.

SCAMMONIÆ RADIX, U. S. P.

(Scammony)

Scammony root is the dried root of *Convolvulus Scammonia*, a perennial herb growing in Western Asia. It contains several glucosids which are closely related to those occurring in jalap. The dose of scammony is from 1 to 10 grains (0.06–0.6 gm.).

PREPARATIONS

DOSE

Resina Scammonii, U. S. P..... 2–5 gr. (0.13–0.3 gm.)
Extractum Colocynthis Compositum, U. S. P.
(14 per cent. of resin)..... 2–10 gr. (0.13–0.6 gm.).

Pharmacologic Action and Therapeutics.—Scammony root has been used as a drastic cathartic since the time of Hippocrates. It is more powerful than jalap, but less irritating than gamboge. It is rarely employed except in the form of the “compound cathartic pill.”

PODOPHYLLUM, U. S. P.

(May Apple, Mandrake)

Podophyllum is the rhizome and roots of *Podophyllum peltatum*, a perennial herb growing in moist shady places in Canada and Northern United States. Its active constituents are a resin and a crystalline principle, *podophyllotoxin*.

PREPARATIONS

Dose

Resina Podophylli, U. S. P. (podophyllin)..... $\frac{1}{8}$ – $\frac{1}{2}$ gr. (0.008–0.03 gm.)
 Fluidextractum Podophylli, U. S. P..... 5–15 min. (0.3–1.0 mil).

Pharmacologic Action and Therapeutics.—In full doses podophyllum is an active, irritant cathartic. It produces its effects slowly, however—rarely earlier than ten or twelve hours after its administration—the evacuations being copious and liquid, and usually attended with much griping pain. It is said to act as a cathartic when applied to an open wound or administered subcutaneously. It was formerly believed to possess the power of directly increasing the secretion of bile, but no reliable evidence can be adduced to support this claim.

Podophyllum is especially prized as a cathartic in *habitual constipation*, associated with so-called “bilious attacks.” To many persons the action of the drug is agreeable, but in others it causes severe pain and depression. When combined with other cathartics only those should be selected which are also slow in action, such as aloes and calomel. Extract of belladonna or hyoscyamus may be added to prevent griping. The resin is the most reliable preparation. A combination such as the following often makes a useful dinner pill:

R_x. Resinæ podophylli..... gr. iv (0.26 gm.)
 Aloes..... gr. xx–xl (1.3–2.6 gm.)
 Extracti nucis vomicæ
 Extracti belladonnæ..... āā gr. iv (0.26 gm.).—M.
 Fiant pilulæ No. xx.
 Sig.—One after dinner or at bedtime.

JALAPA, U. S. P.

(Jalap)

Jalap is the dried tuberous root of *Exogonium Purga*, a perennial herb growing in Mexico. It contains a resin, the chief constituents of which are glucosides similar to those occurring in scammony root. The dose is from 5 to 30 grains (0.3–2.0 gm.)

PREPARATIONS	DOSE
Resina Jalapæ, U. S. P.	1-5 gr. (0.065-0.3 gm.)
Pulvis Jalapæ Compositus, U. S. P. (35 per cent. of jalap and 65 per cent. of potassium bitartrate)	15-60 gr. (1.0-4.0 gm.)
Pilulæ Catharticæ Compositæ, U. S. P. ($\frac{1}{3}$ gr. —0.02 gm.—of extract)	1-3 pills.

Pharmacologic Action and Therapeutics.—Jalap is a drastic hydragogue cathartic. It acts usually within three or four hours, and produces copious watery stools. It not infrequently excites nausea and colic, but its action is less harsh than that of either gamboge or scammony root. Like other cathartics containing resinous active principles, such as podophyllum and colocynth, jalap is less active in the absence of bile, the latter serving as a solvent. Except as an ingredient of compound cathartic pills, jalap is never employed in simple constipation. It is used especially for the removal of *dropsical effusions*, and for this purpose it is usually combined with a saline, as in the official compound jalap powder. Combined with calomel, jalap is sometimes a useful depletive in *decompensated valvular heart disease*, with congestion of the portal system.

ELATERIUM

Elaterium is a substance deposited by the juice of the fruit of *Ecballium Elaterium*, or squirting cucumber, a vine growing on the shores of the Mediterranean Sea. It is of uncertain strength and is not official, but its active properties are fully represented by a neutral principle, *elaterin* (*Elaterinum*, U. S. P.), which is official. The latter occurs in minute white scales or crystals, without odor, and having an acrid, bitter taste. It is insoluble in water, and but sparingly soluble in alcohol. The dose of the parent substance, elaterium, is from $\frac{1}{8}$ to $\frac{1}{2}$ grain (0.008-0.03 gm.).

PREPARATIONS	DOSE
Elaterinum, U. S. P.	$\frac{1}{30}$ — $\frac{1}{10}$ gr. (0.002-0.006 gm.)
Trituratio Elaterini, U. S. P. (10 per cent. with sugar of milk)	$\frac{1}{4}$ —1 gr. (0.016-0.06 gm.)

Pharmacologic Action and Therapeutics.—Elaterium is a decided irritant to all tissues. Given internally it is, perhaps, the most powerful of the drastic hydragogue cathartics, producing large watery stools, with more or less griping, and, occasionally nausea. Its action is more vigorous than that of jalap and less harsh than that of gamboge or colocynth. In over doses it is a violent, acrid poison.

In appropriate doses elaterium is sometimes useful in *local serous effusions* (hydrothorax, hydropericardium, ascites) and the *general dropsy* of cardiac or renal disease. On account of its prompt action, it may be employed also as derivative in *cerebral congestion* and *uremia*. Elaterium itself, probably owing to adulteration, is unreliable, and, therefore, only official preparations should be prescribed.

BRYONIA

Bryonia is the root of *Bryonia alba* and of *Bryonia dioica*, perennial climbing plants growing in central and southern Europe. Its active constituents are resins more and alkaloids. *Bryonin* is merely an impure mixture of these.

PREPARATION	DOSE
Tinctura Bryoniæ.....	1-2 fl. dr. (4.0-8.0 mls).

Bryony is a drastic, hydragogue cathartic. It was formerly a much esteemed remedy in general dropsy and local effusions, but it has been largely superseded by jalap.

FEL BOVIS, U. S. P.

(Ox-gall)

The only preparations of ox-gall used in medicine are the bile salts, sodium glycocholate and sodium taurocholate, which are not official, and the powdered extract, which is official as *Extractum Fellis Bovis*. The latter is an alcoholic extract of bile, evaporated and mixed with starch. The dose of the extract is from 5 to 10 grains (0.3-0.6 gm.); of the salts, 1 to 3 grains (0.06-0.2 gm.), in pills or capsules.

Pharmacologic Action and Therapeutics.—Bile is an active cholagogue and an uncertain laxative. That it is a true hepatic stimulant, increasing both the liquid and solids of the bile has been amply confirmed by Rosenberg, Stadelmann, Joslin, and other investigators who have experimented on both animals and human beings with permanent biliary fistulæ. When bile is not present in the intestines, the digestion of fat is sometimes aided by the administration of ox-gall or bile salts by the mouth. In the test-tube bile suspends peptic digestion by precipitating the soluble proteins (proteoses and peptones) and probably also pepsin; but in the living subject, when the fat is excessive in the stools, it has been shown that it promotes the digestion of proteins.

Careful bacteriologic studies do not indicate that bile possesses the pronounced antiseptic properties that have been

generally attributed to it. It is probable that the fetid character acquired by the stools in the absence of bile is due to impaired intestinal digestion, and, therefore, to better opportunities for the action of bacteria, rather than to the withdrawal of any antiseptic influence exerted directly by the bile itself.

Bile is too uncertain in its action to be employed as an ordinary laxative. In *fecal impaction*, however, an enema containing 2 or 3 per cent. of the extract is often very effective. When, for any reason, the biliary secretion is lacking in the intestine, extract of oxgall may be used as an *adjuvant to certain cathartics*—podophyllum, jalap, colocynth, and scammony—that are ordinarily inactive when bile is not present.

In cases of *biliary fistula* or of *obstruction of the common duct* bile may be used to promote the digestion of fats and proteins, and to prevent, indirectly, putrefactive changes in the intestinal contents. It is best administered in capsules, about two hours after meals. The bile salts, in doses of from 2 to 3 grains (0.13–0.2 gm.), appear to be equally effective.

SULPHUR

(S)

The United States Pharmacopœia recognizes three forms of sulphur:

Sulphur Sublimatum
Sulphur Lotum
Sulphur Præcipitatum.

SUBLIMED SULPHUR (flowers of sulphur) is a fine yellow powder having a slight characteristic odor and a faintly acid taste. It is insoluble in water, but partially soluble in absolute alcohol, ether, chloroform, boiling solutions of alkaline hydrates, oil of turpentine and many other oils. It usually contains small quantities of sulphuric acid, arsenic sulphid, and other impurities. The dose is from $\frac{1}{2}$ to 2 drams (2.0–8.0 gm.). There is one official preparation of sublimed sulphur—the ointment (*Unguentum Sulphuris*, U. S. P.), which contains 15 per cent. of the drug.

WASHED SULPHUR is prepared by digesting for three days sublimed sulphur in weak ammonia water. It enters into (8 per cent.) compound licorice powder (*Pulvis Glycyrrhizæ Compositus*, U. S. P.).

PRECIPITATED SULPHUR (milk of sulphur) is a fine, almost white powder, without odor or taste. It is prepared by precipitating calcium sulphid with diluted hydrochloric acid. The dose is from $\frac{1}{2}$ to 2 drams (2.0–8.0 gm.).

Pharmacologic Action and Therapeutics.—When sulphur is taken internally a considerable portion passes out unchanged; some, however, is transformed into sulphuretted hydrogen and sulphids. It is to these compounds that sulphur owes its active properties. They are the cause of the mild catharsis and the offensive flatus that follow the ingestion of the drug. Being partially absorbed, they escape from the lungs and skin as sulphids, and from the kidneys as sulphates.

Sulphur may be employed as a laxative when a very mild action is desirable, as in *pregnancy, hemorrhoids, fissure of the anus, and prolapse of the bowel*. The dose as a laxative is from 1 to 2 drams (4.0–8.0 gm.) in syrup or molasses. Externally, sulphur is much used as a stimulant and parasiticide in certain chronic diseases of the skin. It is often useful in *eczema, comedo, acne, and psoriasis*, and may be prescribed in an ointment having the strength of from $\frac{1}{2}$ to 2 drams (2.0–8.0 gm.) to the ounce (30.0 gm.). It is absolutely contraindicated in the acute stages of any skin disease. In parasitic diseases, such as *scabies* and *ringworm*, it is a reliable remedy.

HYDRARGYRI CHLORIDUM MITE, U. S. P.

(Mercurous Chlorid, Calomel, Hg_2Cl_2)

Calomel is a white, odorless, tasteless powder, insoluble in all ordinary menstrua. The dose is from $\frac{1}{10}$ to 5 grains (0.0065–0.3 gm.).

PREPARATION

DOSE

Pilulæ Catharticæ Compositæ, U. S. P. (1 gr. —0.06 gm.—of calomel with gamboge, compound extract of colocynth and resin of jalap).....	1–2 pills.
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Pharmacologic Action.—Calomel acts as a laxative or purgative according to the method of its administration and the susceptibility of the patient. These effects are apparently due not to the calomel itself, but to soluble compounds of mercury which are produced in small quantities through the action of the digestive juices and which are mildly irritant to the bowel. The nature of these soluble compounds is not definitely known. It was formerly supposed that calomel was in part transformed into mercuric chlorid by the hydrochloric acid of the stomach, but the investigations of Bucheim, Winkler, and Jeannel proved that such a transformation is impossible at the temperature of the body. It is probable, as Jeannel suggests, that in the presence of the alkaline juices of the intestine the drug is partly converted into an oxid, which is soluble in oily alkaline mixtures, such as are normally present in the duodenum. The effects of calomel,

unlike those of other cathartics, do not increase in direct ratio to the dose, because only small quantities of the drug are transformed into soluble compounds at a time, the greater portion of a large dose being expelled in the feces unchanged. For this reason small doses repeated every hour until 2 grains (0.13 gm.) have been taken, usually operate as freely as a dose of 5 grains (0.3 gm.) taken at once. Calomel stimulates peristalsis chiefly in the upper part of the small intestine and has but little influence on the colon, hence, the usual doses are not always effectual unless they are followed by a saline cathartic. Ordinarily, however, 2 grains (0.13 gm.) in divided doses produce one or two semi-liquid greenish-gray stools in from 10 to 12 hours. The drug does not usually excite much colic, but in some persons its action is accompanied by more or less nausea.

Contrary to what was at one time believed, calomel is not a true cholagogue. There can be no doubt that the amount of bile discharged in the stools is often actually increased under its influence, but the experimental evidence does not favor the view that calomel actually increases the quantity of bile formed by the liver; on the contrary, it indicates that the drug, through its stimulant action on the duodenum, merely speeds the flow of bile through the intestines and lessens to some extent its decomposition. The greenish color of the stools is probably due in part to unchanged bile and in part to sulphid of mercury, and the grayish color to mercurous oxid.

Calomel exerts a slight antiseptic action in the bowel, but doubtless the good effects of the drug in conditions attended with intestinal putrefaction are due less to its power of inhibiting bacterial growth than that of removing through purgation enormous numbers of bacteria with their decomposition products, as well as much undigested food.

Calomel sometimes produces a marked diuretic effect in cardiac dropsy, but the manner of its action is not understood.

Therapeutics.—No remedy is so useful as calomel in the condition commonly called "*biliousness*," which is characterized by a thickly coated tongue, fetid breath, heavy urine, headache, and depression of spirits. A quarter of a grain (0.016 gm.) may be given every half hour until 2 grains (0.13 gm.) have been taken. If the bowels do not move freely, the mercurial may be followed by Epsom salt or a Seidlitz powder. Attacks of *indigestion associated with clay-colored stools*, in either children or adults, are often relieved by a few small doses of calomel. In *dyspeptic diarrhea* it is not quite so efficacious as castor oil in removing undigested food from the bowel, but it has advantages in its tastelessness and small bulk. In the beginning of *acute*

disease, especially the specific infections, it is an excellent cathartic for unloading the bowels without causing undue irritation. In *chronic heart disease* with venous engorgement of the digestive organs calomel is of great value in relieving the tension in the portal circulation, and without its aid digitalis sometimes proves ineffectual.

Administration.—Calomel may be prescribed in the form of a powder or a friable tablet. In accordance with the belief that mercurous chlorid might be converted in the stomach into mercuric chlorid unless an alkali were present, it has been customary to give a few grains of sodium bicarbonate with each dose of calomel, but the combination has no special advantage, for it is now recognized that no mercuric salt is formed in the stomach and that even if it were, the amount of sodium bicarbonate usually employed would have virtually no effect upon the gastric acidity. Ordinarily, it is best to give fractional doses of the drug every hour or half hour until $1\frac{1}{2}$ or 2 grains (0.1–0.13 gm.) have been taken and to follow the last dose in 6 or 8 hours by a saline cathartic.

Massa hydrargyri, U. S. P. (Blue Mass) is made by triturating mercury, 33; oleate of mercury, 1; glycyrrhiza, 10; althæa, 15; glycerin, 9; and honey of rose, 32. It is employed for the same purposes as calomel, although it is less active. The dose is from 3 to 5 grains (0.2–0.3 gm.).

Hydrargyrum cum Creta, U. S. P. (Mercury with Chalk; Gray Powder).—This is an intimate mixture of mercury, honey, and chalk, containing 38 per cent. of mercury. It is slightly weaker than blue mass. The dose is from 3 to 5 grains (0.2–0.3 gm.).

MAGNESII SULPHAS, U. S. P.

(Magnesium Sulphate, Epsom Salt, $\text{MgSO}_4 + 7\text{H}_2\text{O}$)

Magnesium sulphate occurs as small, colorless prismatic crystals or rhombic prisms odorless, and having a bitter saline taste. It is soluble in about 0.8 part of water and is almost insoluble in alcohol. The average dose is 4 drams (15.0 gm.).

PREPARATION

DOSE

Infusum Sennæ Compositum, U. S. P. (12 per cent. of Epsom salt, with senna and manna)..... 2–4 fl. oz. (60.0–120.0 mls).

Pharmacologic Action.—When taken *by the mouth*, magnesium sulphate and other saline cathartics produce their cathartic effect by increasing the amount of fluid in the intestine. They retard the absorption of the fluid in which they were

dissolved and of that taken with food, and also withdraw water from the tissues and blood, the osmotic action continuing until the solution in the bowel becomes isotonic with the blood. The increased bulk and weight of the intestinal contents give an impetus to peristalsis and purgation follows, but there is no direct irritation of the muscular coat of the bowel, as occurs with the vegetable cathartics.

Under ordinary conditions saline cathartics are absorbed from the intestines very slowly and in but small quantities, the greater part escaping from the body in the stools. Their action is, therefore, apparently a purely local one, and this view is supported by the fact that they do not produce catharsis when given intravenously. Saline cathartics, by concentrating the blood, temporarily lessen the secretion of urine; subsequently, however, they may be absorbed from the bowel in sufficient quantity to produce some diuretic effect.

Magnesium sulphate or other salines should not be administered simultaneously with or shortly before the injection of phenol-sulphonaphthalein in making renal function tests, as they decidedly retard the excretion of the dye.

In full doses and in dilute solution magnesium sulphate is an active hydragogue cathartic, producing in the course of a few hours copious watery stools without much colic or systemic disturbance. Concentrated solutions act more slowly than dilute solutions, and, being irritant to the stomach, tend to excite nausea. With very large doses in concentrated solution there is occasionally sufficient absorption of the drug to produce toxic effects. The symptoms of poisoning are extreme muscular weakness, depression of the respiration and circulation, and the excretion of urine having a very high specific gravity (1050–1080).

Administered parenterally, magnesium sulphate and other soluble salts of magnesium are highly toxic, the magnesium ion depressing the heart, the muscles and the entire nervous system, including the peripheral motor nerves. The action of the drug is opposed to that of calcium, although an excess of either the calcium or magnesium ion results in depression of the nervous system and muscles.

Administered subcutaneously (1.5 grams, in 25 per cent. solution, per kilogram of body-weight), magnesium sulphate abolishes the reflexes, relaxes the muscles, and produces unconsciousness and complete surgical anesthesia lasting about 2 hours. Large doses cause death through asphyxia.

Injected into the spinal canal (1 mil of a 25 per cent. solution per 20 lb. of body-weight), the drug produces sensory and motor paralysis of the lower half of the body, the effect occurring in

an hour or two and lasting from 10 to 20 hours. Both subcutaneous and subdural injections are likely to be followed by retention of urine, slight irritation of the kidneys and glycosuria.

Applied directly to an exposed nerve-trunk, a 25 per cent. solution of Epsom salt completely blocks both sensory and motor impulses.

Therapeutics.—Since Epsom salt is free from irritant properties, it is an excellent cathartic for removing undigested material from the bowel in *acute enteritis* and *colitis*. On account of its unpleasant taste and large bulk, however, it is not so convenient for children as calomel, or even castor oil. As it increases the fluidity of the intestinal contents, it is well suited for use in cases of *fecal accumulation*. In *chronic constipation* a saline taken in small dose before breakfast is sometimes more efficacious than a vegetable cathartic. It is an excellent remedy for reducing *dropsical effusions*, both local and general. Magnesium sulphate is an efficient antidote in *acute lead-poisoning*. It forms with the lead salt an insoluble sulphate. It has been recommended also as an antidote in *phenol-poisoning* under the assumption that it would transform the phenol into an innocuous phenolsulphonate, but the combination is effected so slowly that the remedy is virtually useless.

Subcutaneous, intraspinal and intravenous injections of magnesium sulphate have been used to some extent in controlling the convulsive seizures of *tetanus*. While the treatment has yielded good results in some instances, caution must be exercised in applying it, as marked depression of the respiration frequently occurs. Meltzer's recommendations are as follows: Give 3 or 4 times a day through the disease 1.2 mils of a 25 per cent. solution of the drug per kilogram of body-weight by subcutaneous injection. If the convulsive seizures are very severe give 1 mil of a 25 per cent. solution per 20 pounds of body-weight by the intraspinal method. If the disease is attended by immediately dangerous tetanic symptoms, give from 2 to 3 mils per minute of a 6 per cent. solution of Epsom salt by intravenous injection until the dangerous symptoms subside or the respiration becomes shallow or too slow. If the respiration becomes impaired give small amounts of calcium chlorid (2.5 per cent.) intravenously until it shows definite improvement, which may occur in less than 30 seconds. It is also advisable to have at hand an apparatus for intrapharyngeal insufflation in case the respiration becomes very shallow or slow.

In making solutions of magnesium sulphate for parenteral administration only the crystalline salt should be used. Locally, a saturated solution of Epsom salt in the form of a wet compress makes an excellent application in *erysipelas*, *burns of the first*,

second, and third degree, and dermatitis due to ivy or primrose poisoning. It is also effective in acute arthritis, parotitis, epididymitis, neuritis, etc.

Administration.—When a full hydragogue cathartic effect is desired, the drug should be given before breakfast, in one large dose, dissolved in a tumblerful of water. In cases of general dropsy the restriction of liquids after the administration of the salt makes its action still more effective. Solutions of Epsom salt are rendered more acceptable to the stomach by the addition of magnesium carbonate (20–30 gr.—1.3–2.0 gm.). Cathartic enemata are rendered more active by the addition of Epsom salt. The following enema, recommended by Noble, will be found efficacious in cases of marked intestinal torpor:

R. Magnesii sulphatis.....	℥ij (60.0 gm.)
Olei terebinthinæ.....	f℥ss (15.0 mls)
Glycerini.....	f℥j (30.0 mls)
Aquæ.....	q. s. ad f℥iv (120.0 mls).—M.

Incompatibles.—Magnesium sulphate is incompatible with lead acetate, silver nitrate, alkaline carbonates, and lime-water. From solutions of sodium phosphate it precipitates the insoluble magnesium phosphate, and from solutions of Rochelle salt, after a time, the insoluble magnesium tartrate.

MAGNESII OXIDUM, U. S. P.

(Light Magnesia, Calcined Magnesia, Magnesium Oxid, MgO)

Light magnesia is a white, very light, odorless powder, having an earthy taste. It is almost insoluble in water, insoluble in alcohol, but soluble in dilute acids. The dose as a laxative is from 30 to 60 grains (2.0–4.0 gm.).

PREPARATIONS	DOSE
Pulvis Rhei Compositus, U. S. P. (65 per cent.).....	30–60 gr. (2.0–4.0 gm.)
Ferri Hydroxidum cum Magnesii Oxido, U. S. P.....	2–4 fl. oz. (60.0–120.0 mls).

Therapeutics.—Magnesium oxid, or magnesia, is converted in the alimentary canal into soluble salts (chiefly magnesium bicarbonate) that have a laxative action; it therefore combines the properties of an antacid with those of a mild aperient. As an antacid it has about 4 times the neutralizing power of sodium bicarbonate. It is not a suitable drug for habitual use in simple chronic constipation, since, when not thoroughly acidified, there is a possibility of its forming intestinal concretions. It may replace sodium bicarbonate, however, when

excessive acidity exists with constipation. In *ulcer of the stomach* it may be combined with bismuth subcarbonate to control constipation. It may be given with syrup of rhubarb in the early stages of *acute diarrhea* to rid the bowel of any sour, acrid material that may give rise to irritation. It is also an antidote in *poisoning by acids*. Ferric hydroxid with magnesia is used only as an antidote in *poisoning by arsenic* (see p. 301).

MAGNESII OXIDUM PONDEROSUM, U. S. P.

(Heavy Magnesia, Heavy Calcined Magnesia, Magnesium Oxid, MgO)

Heavy magnesia is three and a half times heavier than light magnesia, and, unlike the latter, does not readily unite with water to form a gelatinous hydrate. It has the same properties and uses as light magnesia.

MAGNESII CARBONAS, U. S. P.

(Magnesium Carbonate, $(\text{MgCO}_3)_4 \cdot \text{Mg}(\text{OH})_2 + 5\text{H}_2\text{O}$)

Magnesium carbonate occurs in light, white, friable masses or as a light white powder, free from odor, and having a slightly earthy taste. It is almost insoluble in water, insoluble in alcohol, but soluble in dilute acids with active effervescence. The dose as a laxative is from 20 to 60 grains (1.3–4.0 gm.).

Magnesium carbonate has the same therapeutic value as magnesia, but when there is much acid in the stomach it is likely to cause unpleasant eructations of gas.

MAGMA MAGNESIÆ

(Magnesium Hydroxid, Milk of Magnesia)

Magnesia magma is a thick, white liquid containing magnesium hydroxid in suspension in water. It is prepared by adding a solution of sodium hydroxid to magnesium carbonate in suspension in water. The dose is from 2 to 4 fluidrams (8.0–15.0 mls). It combines the action of a gastric antacid with that of a mild cathartic.

MAGNESII CITRAS

(Magnesium Citrate, $\text{Mg}_3\text{C}_6\text{H}_5\text{O}_7 + 14\text{H}_2\text{O}$)

Magnesium citrate is official as the *Solution of Magnesium Citrate* (Liquor Magnesii Citratis). This preparation is an effervescing solution of magnesium citrate containing a small quantity of sugar and free citric acid. In doses of from 6 to 12 fluidounces (180.0–360.0 mls) it is a pleasant, but somewhat irritating cathartic. It is suitable for occasional use, when it is

desired simply to evacuate the alimentary canal. It should not be employed when there is any inflammation of the gastrointestinal tract.

SODII SULPHAS, U. S. P.

(Sodium Sulphate, Glauber's Salt, $\text{Na}_2\text{SO}_4 + 10\text{H}_2\text{O}$)

Sodium sulphate occurs in large, colorless, transparent prisms, or granular crystals, odorless, and of a bitter, saline taste. It is soluble in 1.5 parts of water. The dose is from 2 to 4 drams (8.0–15.0 gm.).

Therapeutics.—Glauber's salt is a powerful hydragogue cathartic, producing large watery stools, accompanied by griping and borborygmi. Epsom salt, being much less irritating, has largely superseded it. It enters into the mixture known as artificial Carlsbad salt, which makes an efficient mild saline aperient:

R. Sodii sulphatis..... ℥v (150.0 gm.)
 Sodii bicarbonatis..... ℥ij (60.0 gm.)
 Sodii chloridi..... ℥j (30.0 gm.).—M.

Sig.—A teaspoonful in a tumblerful of hot water half an hour before breakfast.

The sulphates of sodium and magnesium are the active ingredients in certain natural mineral waters, such as Hunyadi János, Friedrichshall, Rubinat, and Pullna.

POTASSII ET SODII TARTRAS, U. S. P.

(Potassium and Sodium Tartrate, Rochelle Salt, $\text{KNaC}_4\text{H}_4\text{O}_6 + 4\text{H}_2\text{O}$)

Rochelle salt occurs in colorless, transparent, prismatic crystals, or as a white powder, odorless, and having a cooling, saline taste. It is soluble in less than 1 part of water. The dose is from 1 to 4 drams (4.0–16.0 gm.).

PREPARATION

DOSE

Pulvis Effervescens Compositus, U. S. P. (Seidlitz powder).^{*} 1 powder.

The *blue paper* contains sodium bicarbonate, 40 gr.—2.6 gm.—and potassium and sodium tartrate, 120 gr.—8.0 gm. The *white paper* contains tartaric acid, 35 gr.—2.3 gm. The contents of each paper should be dissolved separately, the two solutions mixed, and the whole taken while effervescing.

Therapeutics.—Rochelle salt may be used as a hydragogue cathartic in the same class of cases in which magnesium

^{*} The present formula was patented by the English chemist Savory in 1815. The powders were named after the mineral spring at Seidlitz, Bohemia, which, however, owes its medicinal properties to sulphates instead of tartrates.

sulphate is indicated. It is less active than the latter salt, but more agreeable to take. Seidlitz powder is a very mild saline cathartic. The carbonic acid evolved during effervescence not only makes the solution palatable, but exerts a sedative influence on the stomach.

SODII PHOSPHAS, U. S. P.

(Sodium Phosphate, $\text{Na}_2\text{HPO}_4 + 12\text{H}_2\text{O}$)

Sodium phosphate occurs in large, colorless, prismatic crystals, odorless, and having a cooling, saline taste. It is soluble in 2.7 parts of water, and insoluble in alcohol. The dose for a young child is from 1 to 10 grains (0.065–0.65 gm.); for an adult, $\frac{1}{2}$ to 4 drams (2.0–15.0 gm.).

PREPARATIONS

DOSE

Sodii Phosphas Effervescens, U. S. P.... 2–4 dr. (8.0–15.0 gm.)

Sodii Phosphas Exsiccatus, U. S. P..... 10–60 gr. (0.65–4.0 gm.).

Therapeutics.—Sodium phosphate in small doses acts as a laxative; in large doses, as a purgative. Its mild action and agreeable taste commend it especially for children, to whom it may be given in milk or other food. It is useful also in the less severe forms of constipation occurring in adults. In *chronic gastric catarrh with constipation* small doses in hot water before meals often have a very beneficial effect not only on the bowel, but also on the stomach. Taken in the same way, sodium phosphate is a valuable depletive in *simple catarrhal jaundice* secondary to duodenitis.

Sodium Acid Phosphate, or sodium biphosphate ($\text{NaH}_2\text{PO}_4, \text{H}_2\text{O}$), occurs as large colorless crystals or a granular powder, having a saline and acid taste. It is readily soluble in water, but is insoluble in alcohol. In large doses it produces a cathartic effect, although it is much more irritant than ordinary sodium phosphate. It is chiefly employed to render alkaline urine acid. The dose is 15 to 20 grains (1.0–1.3 gm.), preferably in lemonade, every two or three hours until the desired effect is produced. It may be given to assist the action of hexamethylenamin, which is not effective in bacteriuria unless the urine is acid.

DIURETICS

Diuretics are agents that increase the flow of urine. They may act (1) by improving the general circulatory condition and relieving passive congestion of the kidneys; (2) by dilating the arterioles of the kidneys; (3) by increasing the water-content of

the blood (salt action); (4) possibly by directly stimulating the renal epithelium.

1. GENERAL CIRCULATORY STIMULANTS.—The chief representatives of this class of diuretics are:

Digitalis

Strophanthus

Squill

Convallaria.

The members of this group have virtually no effect upon the urinary output unless this is reduced owing to impairment of the general circulation. They are particularly useful in decompensated valvular disease with edema.

2. DILATORS OF THE RENAL ARTERIOLES.—Local dilatation of the arterioles of the kidneys, if not accompanied by a reduction of the general arterial pressure, increases the output of urine. The purin derivatives—caffein, theobromin, and theophyllin (theocin)—apparently cause diuresis through a peripheral dilating effect on the renal arterioles.

3. SALINES.—Salts that are readily absorbed from the alimentary canal cause diuresis by drawing water into the blood, thus producing a condition of hydremic plethora and raising the pressure within the capillaries of the glomeruli. Salts that are difficult of absorption, such as magnesium and sulphate ions, draw water into the bowel or inhibit the absorption of water and act as cathartics. The organic salts of sodium, potassium and lithium, and chlorids, nitrates, chlorates, carbonates, bicarbonates and bitartrates owe their diuretic properties to salt action. Chlorids in certain pathologic conditions may accumulate in the tissues and favor the occurrence of edema; for this reason they are not suitable diuretics. Nitrates and chlorates have also an irritant action which unfits them for use. The alkaline carbonates are effective, but, owing to their influence on the gastric acidity, are not usually selected. The bitartrates are absorbed with difficulty and in large doses are cathartic. A portion, however, is absorbed and acts as a diuretic. The lithium salts, at one time very popular, have no advantages over the corresponding potassium salts, and if used freely may excite gastrointestinal inflammation. The most generally useful saline diuretics are:

Potassium citrate

Potassium acetate

Potassium bitartrate.

Dextrose and other sugars, owing to their high osmotic equivalents, also induce diuresis, hence the polyuria of diabetes mellitus. *Urea* produces a similar effect.

4. DIRECT RENAL STIMULANTS.—The most important members of this group are:

Scoparius
Buchu
Uva ursi

Oil of turpentine
Cubeb
Copaiba.

It is possible that these drugs may increase the output of urine by direct stimulation of the renal epithelium, but the results of recent investigations (Cushny, Richards and Plant) are opposed to the theory that urine is separated from the blood by a process of active secretion, and favor the view that filtration is the essential factor in the process, changes in the output of urine depending entirely upon the degree of bloodpressure within the organ. It is probable, therefore, that the direct renal stimulants cause diuresis, not by acting on the secretory cells of the kidney, but by slightly irritating the organ, thus dilating the renal arterioles and increasing the tension within the glomerular capillaries. In large doses these drugs may excite inflammatory changes in the kidneys and decrease the output of urine.

Calomel is sometimes an efficient diuretic, especially if there is general congestion with edema, but whether it acts directly through irritant stimulation or through some effect exerted in the intestines is not definitely known.

With the exception of scoparius and calomel, the direct renal stimulants are not used as diuretics, but chiefly to inhibit bacterial growth in the urine, through their antiseptic properties, and to stimulate the mucous membrane of the urinary passages. They are considered under the heading, "Stimulants to the Urinary Tract."

Diuretics are used for the following purposes:

1. *To Remove Excrementitious Matters from the Blood.*—They are useful for this purpose when the renal function is impaired or suspended, as it often is in acute febrile diseases, in passive congestion of the kidneys, and in some forms of nephritis.

2. *To Promote the Absorption and Excretion of Dropsical Effusion.*—For obvious reasons diuretics are less efficacious in dropsy resulting from organic disease of the kidneys than in that resulting from cardiac insufficiency and general venous stasis.

3. *To Lessen Irritation of the Urinary Passages.*—For this purpose alkaline diuretics are useful when the urine is too concentrated or is excessively acid. They also relieve the distressing symptoms occasioned by uric acid gravel and uric acid stones, not by exercising a solvent action on the concretions, but by producing a more copious secretion of urine.

DIGITALIS, U. S. P.

Digitalis (p. 38) has little or no direct influence on the kidneys, it produces diuresis solely by improving the state of the general circulation, relieving venous congestion of the kidneys, and promoting the absorption of dropsical accumulations. It is preëminently useful in *cardiac insufficiency with oliguria and edema*. In many cases of pronounced dropsy it may be combined advantageously with theobromin or caffein or with one of the saline diuretics. In *nephritis* or *cirrhosis of the liver with dropsy* the action of the drug is usually disappointing, unless there are also evidences of cardiac incompetence. Occasionally, however, the *ascites of hepatic cirrhosis* is favorably influenced by the combination known as Guy's or Niemeyer's pill (see p. 46). In *serous effusions of an inflammatory character*, such as occur in pleurisy and pericarditis, digitalis is of no avail.

STROPHANTHUS, U. S. P.

Strophanthus produces diuresis in the same way as digitalis, but being less certain of absorption, it is much less reliable.

CAFFEINA, U. S. P.

(Caffein)

Caffein is the principal alkaloid of coffee, the seed of *Coffea arabica*, of tea, the dried leaves of *Thea sinensis*, of cola, the seed of *Cola acuminata*, and of guarana, a dried paste prepared from the seed of *Paullina cupana*. As a commercial product it is obtained chiefly from tea. Chemically, it is a methyl derivative of xanthin (trimethylxanthin) and therefore is closely related to theobromin from cacao and theophyllin (theocin) from tea, which are isomeric dimethylxanthins. It appears in the form of colorless, fine, silky crystals, having a bitter taste and a neutral reaction, and soluble in about 46 parts of water. The drug is freely soluble in solutions of sodium benzoate and sodium salicylate, with which compounds it forms double salts.

PREPARATIONS

DOSE

Caffeina Citrata, U. S. P. (a mixture of equal parts of caffein and citric acid).....	2-5 gr. (0.13-0.3 gm.)
Caffeina Citrata Effervescens, U. S. P.....	1-2 dr. (4.0-8.0 gm.)
Caffeinae Sodio-benzoas, U. S. P.....	2-3 gr. (0.13-0.2 gm.).

Pharmacologic Action.—Circulatory System.—The actions of caffein on the circulation are more or less antagonistic to one another. The drug tends to increase the rate of the heart by acting directly on the heart-muscle, and to decrease it by stimulat-

ing the inhibitory center in the medulla oblongata. Again, it tends to raise the arterial pressure (1) by increasing the efficiency of the heart itself, and (2) by stimulating the vasomotor center (vasoconstriction); on the other hand, it tends to lower the arterial pressure by directly dilating the peripheral vessels. The total effect of therapeutic doses, while somewhat variable, is usually to increase the rate of the heart and, also, slightly the output of blood per unit of time.

After toxic doses, in experiments on animals, the cardiac contractions become feeble and arrhythmic, and finally fibrillation of the ventricles ensues and the heart stops in diastole.

Nervous System.—Caffein is an active cerebrospinal stimulant. In man the cerebrum is first affected, then the medulla, and last the spinal cord. Even moderate doses increase mental activity, quicken perception, prevent drowsiness, and lessen the sense of fatigue. In the medulla the drug stimulates the vasoconstrictor, cardio-inhibitory and respiratory centers. In mammals its effects on the spinal cord are seen only after relatively large doses. They are indicated by an increase in the reflex excitability and the occurrence of tetanic convulsions.

Muscles.—Moderate doses of caffeine increase both the irritability and working power of skeletal muscle. Overdoses depress the muscle and eventually bring on a condition of rigor, which is shown by the fibers becoming contracted, hard and opaque.

Respiratory System.—Caffein moderately stimulates the respiratory center, increasing both the depth and frequency of the respirations. There is also some evidence that it causes bronchial dilatation.

Kidneys.—Under favorable conditions caffeine very decidedly increases the output of urine. The increase involves the elimination of water to a much greater extent than that of solids, hence, the specific gravity of the urine falls. The diuretic action of caffeine has been explained in various ways, but it is probably due to peripheral dilatation of the renal arterioles and an increase of pressure in the capillaries of the glomeruli.

Metabolism.—Studies of the effect of caffeine on metabolism have yielded variable results. Small doses of the drug are apparently without influence, while large doses probably increase metabolism slightly.

Absorption and Elimination.—Caffein is readily absorbed, and except in very large doses is without action on the alimentary canal. It leaves the body rapidly, appearing in the urine largely as urea, but partly as dimethyl- and monomethylxanthins. After large doses a small amount is excreted unchanged. Virtually none of the caffeine is transformed into uric acid.

Toxicology.—The chief symptoms of poisoning are restlessness, excitement, anxiety, intense headache, mental confusion, palpitation and precordial distress, followed by tremors and muscular twitchings, embarrassed respiration and collapse. Vomiting and diarrhea may also occur. In the early stages rest, gastric lavage, and the administration of bromids and other sedatives are indicated. Later, the treatment should be that of collapse.

When used too freely as beverages, coffee and tea may cause nervousness, tremors, palpitation, precordial discomfort, insomnia, headache, ready mental and physical fatigue and various digestive disturbances, especially hyperchlorhydria. The empyreumatic oil of coffee and the tannin of tea are probably partly responsible for the disturbed digestion. Individual tolerance to coffee or tea varies considerably. In nervous subjects, however, it is, as a rule, relatively low. The untoward effects of excessive coffee or tea drinking usually disappear rapidly if the habit is discontinued.

Therapeutics.—In *decompensated valvular disease of the heart* caffeine is much less efficacious than digitalis. Moreover, its side actions not rarely prohibit its use. In some cases, however, it is of service as an adjuvant to digitalis, especially when a prompt action is desired or when dropsy is a conspicuous feature. In the *circulatory failure of acute infections, such as pneumonia, typhoid fever*, etc., its action is at times superior to that of digitalis. Owing to its stimulating influence on the cerebrum and medullary centers, it is often of service in combating the depression of *narcotic poisoning*, as by *opium*. While as a diuretic caffeine is especially useful in the *dropsy of cardiac origin*, it may be of service also in effusions resulting from *chronic nephritis* and *cirrhosis of the liver*. In combination with acetphenetidin or a bromid it frequently affords relief in *headache from fatigue* or *nervous strain* and in *migraine*. The manner of its action in these conditions is, however, unknown. In the form of black coffee it is occasionally efficacious in *bronchial asthma*, its good effects probably being due to stimulation of the respiration and relaxation of the bronchi.

Contraindications.—Caffeine is contraindicated in all conditions in which mental excitement or insomnia is a conspicuous feature. In some persons even small doses, if administered late in the day, cause wakefulness at night. Its repeated use as a cerebral stimulant is to be deprecated, as eventually the overwork, which the drug permits, must result in still greater exhaustion of the brain. The drug should not be used as a diuretic in cases of acute nephritis.

Administration.—As caffeine and citrated caffeine are readily decomposed in the presence of water, they are usually prescribed

for internal use in pills, capsules, or powders. When a prompt action is desired the drug should be given hypodermically, and for this purpose the sodio-benzoate of caffein is a suitable preparation, as it is freely soluble in water and quite stable in solution.

THEOBROMINA

(Theobromin).

Theobromin is an alkaloid obtained from the seeds of *Theobroma Cacao*, or chocolate tree, extensively grown in South America and the West Indies. It is also produced synthetically. It occurs in minute white crystals, of a bitter taste, and sparingly soluble in water. The dose is from 3 to 8 grains (0.2–0.5 gm.). Two double salts of theobromin are recommended because of their ready solubility in water, namely, *theobromin sodio-salicylate*, or *diuretin* (Theobrominae Sodio-salicylas, U. S. P.) and *theobromin sodio-acetate*, or *agurin*, but for administration by the mouth they offer no advantages over the pure alkaloid. They undergo decomposition upon exposure to the air and are incompatible with acids. Either salt may be given in doses of from 5 to 15 grains (0.3–1.0 gm.) dissolved in peppermint-water or in capsules.

Pharmacologic Action.—Theobromin belongs to a group of compounds which are known as purins. Xanthin is dioxypurin, theobromin and caffein are dimethylxanthin and trimethylxanthin respectively, and theophyllin (theocin) is also a dimethylxanthin. Theobromin acts similarly to caffein, but it has much less influence on the central nervous system than the latter and is relatively weak as a cardiac stimulant. It is excreted in the urine partly unchanged and partly as heteroxanthin.

Therapeutics.—Theobromin may be used as a *diuretic* in the same class of cases as caffein. It has an advantage over the latter in being less stimulating to the psychic functions. In *cardiac insufficiency with edema* it is often an excellent adjuvant to digitalis. In *chronic nephritis*, when degeneration of the kidneys is far advanced, like other diuretics it is frequently ineffectual in removing the dropsy, but in some cases it gives good results, especially when the patient is kept for a few days on the Karel diet. Theobromin is a favorite drug with French clinicians in warding off attacks of *angina pectoris*, its good effects being ascribed to relaxation of the coronary arteries.

When given continuously theobromin is prone to lose its diuretic effect somewhat rapidly, and therefore it is advisable not to use it for more than 2 or 3 days at a time.

THEOPHYLLINA, U. S. P.

(Theophyllin, Theocin)

Theophyllin is a xanthin derivative isomeric with theobromin (dimethylxanthin). It is present in small quantities in tea (*Thea sinensis*) and is also prepared synthetically. The official product is a white crystalline powder, with a bitter taste, and soluble in about 100 parts of water. The dose is from 3 to 8 grains (0.2–0.5 gm.), in hot liquid, after meals. Theophyllin sodium-acetate (*Theophyllinæ Sodio-acetas*), or soluble theophyllin, containing 60 per cent. of the alkaloid, is also in use.

Theocin is a powerful diuretic, but its effects are somewhat evanescent, rarely lasting more than a few days. Like theobromin, it has little influence on the central nervous system, but it is more effective as a diuretic than either theobromin or caffein, and is even more stimulating to the heart than the latter. It may be employed in *dropsy* from any cause, except that of acute nephritis. In *cardiorenal disease* it may often be prescribed advantageously with digitalis. To secure the best results theocin should be intermitted every few days, and an alkaline diuretic substituted. The drug is usually well borne, but sometimes it causes nausea or vomiting, headache and vertigo.

CONVALLARIA

The action of convallaria resembles that of digitalis. While the drug has advantages in not having any cumulative effect and in not often disturbing the stomach, it is distinctly inferior to digitalis, both as a circulatory stimulant and as a diuretic, owing to the uncertainty of its absorption.

SCILLA, U. S. P.

(Squill)

Squill has an action on the circulation similar to that of digitalis, although it is much less effective, owing to poor absorption. Like digitalis it acts indirectly as a diuretic by improving the circulation and relieving general venous congestion. Large doses of the drug cause vomiting and purging.

Squill is employed chiefly as an expectorant (see p. 287) and as a diuretic. For the latter purpose it is rarely given by itself, but in combination with digitalis. Reference has already been made to the usefulness of a combination of digitalis, squill, and blue mass in some cases of *cardiac* and *hepatic dropsy*. Squill is contraindicated in acute nephritis.

SCOPARIUS

(Broom)

Scoparius is the tops of *Cytisus Scoparius*, a shrub indigenous to Western Asia and Southern Europe, and cultivated in the United States. It contains a liquid alkaloid, *spartein*, and a neutral principle, *scoparin*. The salts of spartein, of which the sulphate is official, are crystalline solids. Scoparin is rarely used.

PREPARATIONS

DOSE

Fluidextractum Scoparii.....	½-1 fl. dr. (2.0-4.0 mls)
Decoctum Scoparii (1 oz. to 1 pint—30.0 gm. to 0.5 L.).....	1-3 fl. oz. (30.0-90.0 mls).

Pharmacologic Action and Therapeutics.—The chief effect of moderate doses of scoparius is an increase in the flow of urine. The diuresis is not due to the spartein, which has an action similar to that of coniin (see p. 158), but to the scoparin, which probably acts directly on the kidney. Large doses cause vomiting and purging. Scoparius, alone or with digitalis, is sometimes efficacious in *cardiac dropsy*. The decoction is generally employed.

ORGANIC SALTS OF POTASSIUM

Pharmacologic Action.—In very large doses potassium is a depressant to both the nervous system and the circulatory system, especially to the latter. In the case of the organic salts of potassium, however, the action of the base is subordinate to that of the acid radical, and a depressant effect is never observed except after a very large dose of the salt or after its prolonged administration. The chief effect of a moderate dose of any one of the organic salts of potassium is an increased secretion of urine. The mineral salts of the urine, both of potassium and sodium, are increased, but the evidence is not convincing that the salts of potassium hasten oxidation in the tissues, and in consequence augment nitrogenous elimination. In large doses they impart an alkaline reaction to the urine.

Therapeutics.—The organic salts of potassium and other mild alkalis may often be combined advantageously with salicylates in the treatment of *acute rheumatism*. It is doubtful whether they exert any direct influence on the disease itself, but apparently they lessen the tendency of the salicylates to irritate the stomach and kidneys. They are useful adjuvants to colchicum and cinchophen in the treatment of *gout*, but the manner of their action is not apparent. It is certain, however, that they do not

act by hindering the formation of uric acid or by increasing its solubility in the tissues.

Alkalis or mineral waters containing them are apparently of service in *acute catarrh of the bile-ducts* and in *cholelithiasis*, probably by relieving coexisting duodenal catarrh, and not by exerting any direct influence on the bile itself or its concretions. They are also useful in relieving *dysuria* that is due to *excessive acidity of the urine*, and through their diluent action they tend to mitigate the suffering occasioned by *uric acid gravel* and *uric acid calculi*. In *acute nephritis* they serve to maintain the excretion through the kidneys and to render the urine less irritating. In many cases of *pyelitis due to the colon bacillus* the mild alkaline salts of potassium give better results than hexamethylenamin. Potassium citrate may be selected and given to adults in doses of 20 to 30 grains (1.3–2.0 gm.), four times a day, or to infants in doses of 10 to 15 grains (0.6–1.0 gm.), four times a day. The exact amount may be determined by testing the reaction of the urine. Not rarely it is advisable to employ hexamethylenamin and alkalis in alternating courses.

Finally, the organic salts of potassium are efficient sedative expectorants in the beginning of *acute bronchitis*, especially when the secretion is viscid and scanty.

Incompatibles.—The organic salts of potassium are incompatible with acids, mineral salts, and alkaloidal salts.

POTASSII BICARBONAS, U. S. P.

(Potassium Bicarbonate, KHCO_3)

Potassium bicarbonate occurs as colorless prismatic crystals or as a white granular powder, odorless, and having a saline, alkaline taste. It is soluble in about 3 parts of water and almost insoluble in alcohol. The dose is from 10 to 30 grains (0.65–2.0 gm.) in solution well diluted. On account of its unpleasant taste and neutralizing effect on gastric acidity, it is less frequently prescribed than the citrate and acetate of potassium.

POTASSII CARBONAS, U. S. P.

(Potassium Carbonate, K_2CO_3)

Potassium carbonate is a white, granular, deliquescent powder, alkaline in reaction, and caustic to the taste. It is freely soluble in water, but insoluble in alcohol. The dose is from 10 to 30 grains (0.65–2.0 gm.), but on account of its irritant properties it is not used internally.

POTASSII BITARTRAS, U. S. P.

(Potassium Bitartrate, Cream of Tartar, $\text{KHC}_4\text{H}_4\text{O}_6$)

Potassium bitartrate occurs as colorless or slightly opaque, rhombic crystals, or as a white powder, odorless, and of an acidulous taste. It is soluble in about 150 parts of water, and very sparingly soluble in alcohol. The dose is from 15 to 60 grains (1.0–4.0 gm.).

PREPARATION

DOSE

Pulvis Jalapæ Compositus, U. S. P. (jalap, 35;
potassium bitartrate, 65)..... 15–60 gr. (1.0–4.0 gm.).

Unlike the other organic salts of potassium, the bitartrate and tartrate are not readily absorbed from the digestive tract and consequently in large doses they are cathartic. A portion, however, is absorbed and this has a diuretic effect. When introduced directly into the circulation tartrates are capable of producing a severe tubular nephritis, but when taken by the mouth in ordinary doses they have no irritant action on the kidneys. Indeed, the bitartrate is often used in *acute nephritis* to promote diuresis and to lessen the acidity of the urine. The following combination, known as imperial drink, is pleasant, and may be given freely in *typhoid fever* and other acute infections to supply water and to promote diuresis:

Potassium bitartrate.....	1½ drams (6.0 gm.)
Sugar.....	½ ounce (15.0 gm.)
Grated lemon-peel.....	½ ounce (15.0 gm.)
Boiling water.....	2 pints (1.0 L.).

POTASSII ACETAS, U. S. P.

(Potassium Acetate, $\text{KC}_2\text{H}_3\text{O}_2$)

Potassium acetate occurs as a white powder or as crystalline masses, very deliquescent, odorless, and of a saline taste. It is soluble in 0.5 part of water or in 3 parts of alcohol. The dose is from 15 to 60 grains (1.0–4.0 gm.). On account of its ready solubility, pleasant taste, and freedom from irritant properties, potassium acetate is a favorite alkaline diuretic.

POTASSII CITRAS, U. S. P.

(Potassium Citrate, $\text{K}_3\text{C}_6\text{H}_5\text{O}_7 + \text{H}_2\text{O}$)

Potassium citrate occurs in transparent, prismatic crystals or white, granular powder, deliquescent on exposure to air, odorless, and having a pleasant saline taste. It is soluble in 0.6

part of water, but sparingly soluble in alcohol. The dose is from 15 to 60 grains (1.0–4.0 gm.).

PREPARATIONS

DOSE

Liquor Potassii Citratis, U. S. P. (8 per cent. of potass. cit.).....	$\frac{1}{2}$ –1 fl. oz. (15.0–30.0 mls)
Potassii Citras Effervescens, U. S. P.....	30–90 gr. (2.0–6.0 gm.).

The citrate of potassium has properties closely resembling those of acetate of potassium, and the two salts may be used interchangeably. Owing to its more agreeable taste, however, it is usually preferred to other organic salts of potassium as a *sedative expectorant* and *alkaline diuretic*. The solution of potassium citrate is used in *mild febrile conditions* to promote the secretion of the skin and kidneys.

POTASSII NITRAS, U. S. P.

(Potassium Nitrate, Saltpeter, KNO_3)

Potassium nitrate occurs as colorless, transparent, rhombic prisms, or as a crystalline powder having a cooling, saline taste. It is permanent in the air. It is soluble in 2.8 parts of water, and sparingly soluble in alcohol. The dose is from 5 to 20 grains (0.3–1.3 gm.), in solution, well diluted.

Pharmacologic Action.—Potassium nitrate has an action similar to that of the organic salts of potassium, but it is more irritant to the gastrointestinal tract. Its diuretic effect is the result of salt action. The drug is excreted unchanged and for the most part in the urine.

Toxicology.—Toxic doses produce the symptoms of severe gastro-enteritis, with oliguria and hematuria, or with complete suppression of the urine. *Treatment* consists of gastric lavage and the administration of demulcents and copious draughts of water.

Therapeutics.—Potassium nitrate was formerly used as a diuretic in *general dropsy*, but it has been supplanted by the organic salts of potassium, which are much less irritant. Inhalation of the smoke of burning niter paper is sometimes effective in *bronchial asthma*. On burning the nitrate is reduced to a nitrite which has relaxing influence on the bronchial muscles.

POTASSII CHLORAS, U. S. P.

(Potassium Chlorate, KClO_3)

Potassium chlorate occurs in the form of colorless, crystalline plates, odorless, and of a cooling saline taste. It is soluble in 11.5 parts of water, and sparingly soluble in dilute alcohol.

The dose is from 3 to 10 grains (0.2–0.65 gm.), in solution, well diluted.

PREPARATION

DOSE

Trochisci Potassii Chloratis, U. S. P. (each contains about $2\frac{1}{2}$ gr.—0.15 gm.)..... 1–4 troches.

Pharmacologic Action.—When applied in dilute form to mucous membranes, potassium chlorate acts as an antiseptic, stimulant, and astringent; in concentrated form it is decidedly irritant. When taken internally it does not, as was formerly believed, yield its oxygen to the blood, but it passes out of the body unchanged. Most of it—more than 90 per cent.—escapes in the urine, but, according to Isambert, small quantities can be recovered from the saliva, the tears, and the milk of nursing women. The only appreciable effect of moderate doses, well diluted, is an increase in the flow of urine. Concentrated solutions, even of therapeutic doses, give rise to a burning sensation in the stomach, followed by nausea and vomiting. Jacobi was the first to point out that the practice of giving the drug internally in large doses was a dangerous one, and to prove that many deaths that had been attributed to other causes were in reality due to potassium chlorate poisoning.

Toxicology.—The symptoms of potassium chlorate poisoning are the resultant of the drug's irritant action on the gastrointestinal tract and kidneys and its power to transform the hemoglobin of the blood into methemoglobin and to destroy the corpuscles. The first symptoms are thirst and abdominal pain, followed by vomiting and purging. Cyanosis is almost constantly present, and is accompanied by dyspnea and the usual phenomena of cardiac failure. The urine is scanty, dark colored, and albuminous, and on microscopic examination reveals numerous pigmented tubercasts and granular detritus derived from the red blood-cells. Jaundice is often present, and in many cases death is preceded by coma and convulsions. The immediate cause of death may be heart failure, asphyxia, or uremia, according as the action of the poison has been most pronounced on the circulation, blood, or kidneys. Apart from gastro-enteritis and nephritis, the most striking postmortem change is that which involves the blood. The color of the blood is changed to a chocolate hue, oxyhemoglobin is replaced by methemoglobin, and many of the red cells are decolorized and more or less disintegrated. The organs generally may be chocolate colored from the accumulation in the tissues of liberated blood-pigment. In the recorded cases the minimum fatal dose for an adult has been 4 drams; for a child of four years, 3 drams; and for an infant, 1 dram.

The *treatment of poisoning* consists in evacuating the stomach and in administering demulcents and diluents. Subcutaneous injections of normal saline solution may be tried.

Therapeutics.—Potassium chlorate makes an excellent local application in inflammatory affections of the mouth and throat. Thus, it is valuable in the various forms of *stomatitis* and in *acute pharyngitis*. In these affections a solution of from 10 to 20 grains (0.65–1.3 gm.) to the ounce (30.0 mls) may be used as a wash or gargle. In acute pharyngitis tannin or some preparation containing it is frequently added to the solution.

In *scarlatina* and *diphtheria* it is advisable to avoid solutions of potassium chlorate, and to select an agent that, if swallowed, will not contribute to the existent renal irritation. In *ulcerous stomatitis* this salt is almost a specific, and may be used internally as well as locally. The dose for a child of three years is from 1 to 2 grains (0.06–0.13 gm.), well diluted, every three hours. Benefit from its internal administration is to be attributed to its continuous elimination in the saliva. Tincture of ferric chlorid may be used as an adjuvant, as in the following formula:

℞. Potassii chloratis..... gr. xxx (2.0 gm.)
 Tincturæ ferri chloridi..... ℥xxxij (2.0 mls)
 Syrupi zingiberis..... f ʒss (15.0 mls)
 Aquæ..... q. s. ad f ʒij (60.0 mls).—M.

Sig.—A teaspoonful in water every three hours.

It is generally believed that *salivation* is less likely to result from the continuous use of mercury when a solution of potassium chlorate is used at the same time as a mouth-wash. In some cases of *syphilis* troches of the salt are useful as preventives of both mercurial stomatitis and of mucous patches.

Incompatibles.—Owing to rapid oxidation or reduction violent explosion may occur when potassium chlorate is triturated with such substances as tannic acid, phosphorus, pulverized charcoal, sulphur, sulphids, sugar, hyposulphites, hypophosphites, and ammonium chlorid. Mixtures of potassium chlorate, tincture of ferric chlorid, and glycerin, when warm, are liable to explode. The salt reacts with strong hydrochloric acid, setting free chlorin gas; with potassium iodid it may form the exceedingly irritant potassium iodate, and from syrup of ferrous iodid it may precipitate free iodin.

LITHII CARBONAS, U. S. P.

(Lithium Carbonate, Li_2CO_3)

Lithium carbonate occurs as a white powder, odorless, and of an alkaline taste. It is soluble in 78 parts of water and insoluble in alcohol. Its dose is from 5 to 20 grains (0.3–1.3 gm.).

Pharmacologic Action and Therapeutics.—The salts of lithium have actions similar to those of the corresponding salts of potassium. Like the latter, they increase the output of urine and lessen its acidity. When used continuously, however, they are likely to cause irritation of the gastrointestinal tract. Lithium salts were originally recommended in the treatment of *gout*, because it was found that outside of the body lithium united with uric acid to form a more soluble salt than either sodium or potassium, but it has clearly demonstrated that no alkaline medication has any influence on the urates present in the blood or tissues. Any efficacy that the natural “lithia waters” may possess in the treatment of gout or nephrolithiasis is dependent upon the water itself and not upon the traces of lithium salts contained in them.

LITHII CITRAS, U. S. P.

(Lithium Citrate, $\text{Li}_3\text{C}_6\text{H}_5\text{O}_7 + 4\text{H}_2\text{O}$)

Lithium citrate is a white, deliquescent powder, odorless, and of a cooling, alkaline taste. It is soluble in 1.4 parts of water and almost insoluble in alcohol. Its dose is from 5 to 20 grains (0.3–1.3 gm.).

Lithium citrate is the therapeutic equivalent of lithium carbonate.

LITHII BENZOAS

(Lithium Benzoate, $\text{LiC}_7\text{H}_5\text{O}_2$)

Lithium benzoate occurs in the form of a white powder or small shining scales, permanent in the air, odorless, and of cooling, sweetish taste. The dose is from 5 to 20 grains (0.3–1.3 gm.).

This drug was recommended in the treatment of *gout* on the ground that it would prove especially active as a uric acid solvent, the acid radical uniting with protein derivatives to form the soluble hippuric acid, and the basic radical uniting with free uric acid to form a readily soluble urate. This assumption, however, has been shown to be fallacious by recent studies on uric acid formation and elimination, and moreover, in practice, lithium benzoate has been found to be even less efficacious in gouty conditions than the other salts of lithium.

OTHER DIURETICS

Calomel (see p. 229).—This drug is sometimes an effective diuretic in *cardiac disease with dropsy*, but whether it acts directly through irritant stimulation of the kidneys or indirectly through its action on the intestines is not definitely known. A few large

doses (2–3 gr.—0.13–0.2 gm.) may be given, opium being added, when necessary, to prevent purging; or small doses ($\frac{1}{4}$ gr.—0.016 gm.) may be employed as adjuvants to digitalis and squill.

Spirit of Nitrous Ether (see p. 275).—Sweet spirit of niter is an agreeable remedy of feeble diuretic power. Each of its components—ethyl nitrite, ether, and alcohol—probably contributes to its activity. It is useless in general dropsy, but it is sometimes of service in relieving *oliguria* that is due to *febrile disease* or *active congestion of the kidneys*. The usual dose for an adult as a diuretic is from 1 to 2 fluid drams (4.0–8.0 mls) and for a child of 1 year 5 to 10 minims (0.3–0.6 mil).

Incompatibles.—Spirit of nitrous ether is incompatible with antipyrin, iodids, ferric sulphate, tincture of guaiacum, mucilage of acacia, and tannic acid.

STIMULANTS TO THE URINARY TRACT

Under this heading will be considered those drugs that stimulate the mucous membrane of the whole urinary tract. All of them in ordinary doses increase the output of urine by slightly irritating the kidneys and dilating the renal arterioles, but this diuretic effect is subordinate to that exerted upon the mucous membranes over which the urine flows. Many of them contain antiseptic principles that are eliminated by the kidneys, and that are powerful enough to inhibit the growth of bacteria and to prevent decomposition of the urine. In large doses these drugs are capable of producing acute inflammation of the bladder and urethra, and even of the kidneys themselves.

The most important members of this group are:

Copaiba	Oil of erigeron
Cubeb	Buchu
Matico	Uva ursi
Oil of sandalwood	Sabal
Oil of turpentine	Pareira
Juniper	Cantharides.

The combined stimulant and antiseptic properties of these drugs make them useful remedies in subacute and chronic pyelitis, cystitis, and urethritis. They are contraindicated when the inflammation is of an acute character.

COPAIBA, U. S. P.

(Balsam of Copaiba, Copaiva)

Copaiba is the oleoresin of *Copaiba Langsdorffi* and other species of *Copaiba*, a small tree growing in the northern states of

South America. It is a yellowish or brownish viscid liquid, having a peculiar, aromatic odor and a bitter, acid taste. It contains a volatile oil (40.9 per cent.), resins, a bitter principle, and copaivic acid. The dose of copaiba is from 5 to 30 minims (0.3–2.0 mils) in capsule or emulsion.

PREPARATION	DOSE
Oleum Copaibæ.....	5–15 min. (0.3–1.0 mil).

Pharmacologic Action and Therapeutics.—In therapeutic doses copaiba acts as a stimulant to mucous membranes. As its active principles are eliminated chiefly by the kidneys and lungs, it particularly influences the mucous membrane of the genito-urinary tract and bronchi. The drug also excites diuresis, and imparts to the urine antiseptic properties. The resins and most of the oil are excreted by the kidneys, but a small part of the oil escapes through the lungs and skin. The oil appears in the urine in part unchanged, and in part in combination with glycuronic acid. Urine containing the resins of copaiba responds to the nitric acid test for albumin, but the resinous precipitate can be distinguished by its rapid disappearance on the addition of alcohol. Fehling's solution may also be reduced by urine containing the educts of copaiba. In large doses copaiba acts as an irritant, causing burning in the stomach, vomiting and purging, lumbar pains, frequent micturition, and even strangury. In some persons the administration of the drug is followed by an eruption on the skin, urticarial, scarlatinoid, or morbilliform in type.

In inflammatory diseases of the urinary tract, such as *pyelitis*, *cystitis*, and *urethritis*, copaiba is a useful remedy; it should not be used, however, until the most acute symptoms have subsided. In *gonorrhea*, after the discharge has become well established, the drug affords considerable relief and tends to prevent complications. It may be combined advantageously with other drugs, such as cubeb and salol, which tend to render the urine sterile. In *subacute and chronic bronchitis* with profuse purulent expectoration it is sometimes beneficial, but generally it is less useful than terebene, eucalyptol or the preparations of guaiacol. Copaiba has a long-standing reputation as a stimulant application for *indolent ulcers*.

Both copaiba itself and the oil are eligible preparations. On account of their unpleasant taste they should always be prescribed in capsules or as an emulsion.

CUBEBA, U. S. P.

(Cubeb)

Cubeb is the dried unripe fruit of *Piper Cubeba*, a perennial climber indigenous to Borneo and the adjacent islands. It

contains a volatile oil (5–15 per cent.), a resin, cubebic acid, and cubebin, which is inert. The dose of powdered cubeb is from $\frac{1}{2}$ to 2 drams (2.0–8.0 gm.).

PREPARATIONS	Dose
Oleoresina Cubebæ, U. S. P.	5–15 min. (0.3–1.0 mil)
Oleum Cubebæ, U. S. P.	5–15 min. (0.3–1.0 mil)
Trochisci Cubebæ, U. S. P. (each contains about $\frac{1}{3}$ gr. (0.02 gm.) of oleoresin)	1–5 troches.

Pharmacologic Action and Therapeutics.—Cubeb possesses properties closely resembling those of copaiba; hence it may be employed to meet the same indications as the latter. A combination of the two is often more effective than either alone. Cubeb is somewhat less likely than copaiba to disturb digestion or to cause cutaneous rashes. Troches of cubeb are useful in relieving hoarseness and fatigue of the larynx resulting from prolonged use of the voice. The oleoresin is the most active preparation; it should be given in capsules or as an emulsion.

MATICO

Matico is the leaves of *Piper angustifolium*, a shrub growing in Mexico and South America. It contains a volatile oil, a resin, tannin, and artanthic acid.

Pharmacologic Action and Therapeutics.—Matico somewhat resembles cubeb in its action, and has been given in the same class of cases. The leaves, on account of their hairy surfaces, favor coagulation and arrest bleeding when applied to small wounds. The drug is rarely employed at the present time.

OLEUM SANTALI, U. S. P.

(Oil of Santal, Oil of Sandalwood)

Oil of santal is a volatile oil distilled from the wood of *Santalum album*, a small tree growing in India and the East Indian Islands. It is a thick, pale-yellow liquid, having a strong, aromatic odor and a pungent, spicy taste. It is soluble in alcohol. The dose is from 5 to 20 minims (0.3–1.2 mils), in capsules or as an emulsion.

Oil of santal resembles copaiba in its action, but is less irritant.

TEREBINTHINA

(Turpentine)

Turpentine is a concrete oleoresin obtained from *Pinus palustris* and other species of *Pinus* growing in the Southern United

States, especially in North Carolina. When subjected to distillation it yields a volatile oil, *Oleum Terebinthinæ*, and a solid residue, *resin*.

OLEUM TEREBINTHINÆ, U. S. P.

(Oil of Turpentine, Spirit of Turpentine)

Oil of turpentine is a limpid, colorless, highly inflammable liquid, having a characteristic odor and taste. It contains several terpene hydrocarbons. The rectified oil is made by distilling the ordinary oil with lime-water, and is the preparation always selected for internal use.

PREPARATIONS	DOSE
Oleum Terebinthinæ Rectificatum, U. S. P.	5-20 min. (0.3-1.2 mls)
Emulsum Olei Terebinthinæ, U. S. P. (15 per cent.)	$\frac{1}{2}$ -2 fl. dr. (2.0-8.0 mls)
Linimentum Terebinthinæ, U. S. P. (oil of turpentine, 35; resin cerate, 65).	

Terpin hydrate (see p. 295) is a crystalline compound obtained by the interaction of oil of turpentine, alcohol, and nitric acid.

Terebene (see p. 295) is a liquid hydrocarbon made by oxidizing oil of turpentine with strong sulphuric acid.

Pharmacologic Action.—When applied to the skin, oil of turpentine acts as an irritant, producing redness and burning, and, if the contact be prolonged, vesication. The drug has decided antiseptic properties, and is capable, even in dilute form, of preventing fermentation and putrefaction. Internally, in full doses, it causes a sense of warmth in the stomach, quickened respiration, and an increase in the rate of the pulse. It is excreted chiefly by the kidneys as terpenals, but a small portion leaves the body through lungs. It imparts to the urine an odor resembling that of violets. In overdoses the drug produces abdominal pain, nausea, vomiting, embarrassed respiration, a rapid, feeble pulse, great muscular relaxation, lumbar pains, dysuria, scanty bloody urine, delirium, and finally coma.

In therapeutic doses oil of turpentine acts as a carminative, diuretic, urinary antiseptic and expectorant. In susceptible persons an erythematous or papular eruption may result from either its internal or its external use.

Therapeutics.—Externally oil of turpentine is used as a rubefacient in various inflammatory affections, such as *bronchitis*, *pleurisy*, *pneumonia*, *gastritis*, and *enteritis*. It is best applied in these cases in the form of a stupe made by sprinkling freely with the oil a piece of flannel which has first been soaked in boiling water and then wrung dry. It may be allowed to remain on the affected part from ten to twenty minutes, according to

the sensitiveness of the skin. Turpentine liniment makes an excellent application in *myalgia* and *chilblains*.

Oil of turpentine is a reliable carminative, and may be administered either by the mouth or by the rectum. Troublesome *tympanites* will often yield to the application of a stupe to the abdomen and the rectal injection of a pint of soapy water containing a tablespoonful of the oil.

The oil is a valuable adjunct to alcohol in certain cases of *typhoid fever*. It is useful when the tongue is dry, brown, and fissured; when there is a tendency to muttering delirium; and when there is marked abdominal distention. It sometimes acts favorably as a stimulant and antiseptic in subacute and chronic inflammations of the genito-urinary tract, such as *cystitis* and *urethritis*. It may be employed as an expectorant in *subacute and chronic bronchitis*, when the expectoration is copious and purulent, but generally terebene will be found more agreeable. With some practitioners it has acquired a reputation as a hemostatic in *passive hemorrhage* from the stomach, intestines, lungs, or kidneys. Some cases of *purpura hæmorrhagica* seem to be favorably influenced by the oil.

Oil of turpentine, $\frac{1}{2}$ to 1 fluidounce (15.0–30.0 mls), with castor oil, has been used as an anthelmintic to remove *tape-worm*, but there are other remedies more effective and decidedly less dangerous.

Oil of turpentine is a powerful deodorant. In the form of vapor it may be employed to overcome the fetid odor of the breath in *bronchiectasis* and *gangrene of the lung*. It is serviceable for removing the odor from the hands after postmortem examinations. Madden has found it efficacious in destroying the offensive character of the discharges in *carcinoma of the uterus*. He recommends a douche composed of a tablespoonful each of the oil and magnesia to a quart of boiling water; the mixture is to be cooled and thoroughly stirred before being used. The penetrating odor of iodoform is lost to some extent in the presence of turpentine.

Whatever may have been the merits of old preparations of the oil in *phosphorus-poisoning*, it is certain that the present article of commerce is entirely without efficacy.

Contraindications.—It should not be prescribed when there is acute inflammation of the stomach, intestines, or genito-urinary tract.

Administration.—Oil of turpentine may be administered on lumps of sugar, in capsules, or in emulsion.

Incompatibles.—Bromin, iodin, nitric acid, and strong sulphuric acid act with violence on oil of turpentine.

RESINA, U. S. P.
(Rosin, Resin, Colophony)

Rosin is the hard, transparent, amber-colored residue left after distilling off the volatile oil from turpentine.

PREPARATIONS

Ceratum Resinæ, U. S. P. (rosin, 35 parts; yellow wax, 15 parts; lard, 50 parts).

Emplastrum Resinæ (rosin, 14 parts; lead-plaster, 80 parts; yellow wax, 6 parts).

Therapeutics.—Rosin cerate is chiefly employed as a stimulating application for *indolent ulcers*. Rosin plaster is less irritating to the skin than the rubber adhesive plaster, and is to be preferred to the latter for strapping the chest in fracture of the ribs and in pleurisy, and for making compression over indolent ulcers.

JUNIPERUS

(Juniper)

Juniper is the fruit of *Juniperus communis*, an evergreen shrub growing in Northern Europe, Asia, and America. It contains a volatile oil and a resin.

PREPARATIONS

DOSE

Oleum Juniperi, U. S. P.	3-5 min. (0.2-0.3 mil)
Spiritus Juniperi, U. S. P. (5 per cent. of oil of juniper)	½-1 fl. dr. (2.0-4.0 mls)
Spiritus Juniperi Compositus, U. S. P. (equivalent to gin)	1-4 fl. dr. (4.0-15.0 mls).

Pharmacologic Action and Therapeutics.—Juniper is a more active diuretic than most of the stimulants to the urinary tract. The compound spirit is useful in increasing the flow of urine in *passive congestion of the kidneys* resulting from chronic heart disease. Its combination with an organic salt of potassium enhances its effect. In subacute and chronic inflammatory diseases of the urinary tract it is not generally so useful as copaiba, oil of santal, or buchu.

OLEUM ERIGERONTIS

(Oil of Erigeron, Oil of Fleabane)

Oil of erigeron is a volatile oil distilled from the fresh, flowering herb of *Erigeron canadensis*, an annual shrub growing in waste places in North America. It is a pale-yellow liquid, having a persistent aromatic odor and taste. The dose is from 5 to 15 minims (0.3-1.0 mil), on sugar, in capsules, or as an emulsion.

Oil of erigeron resembles oil of turpentine in its action, but it is less powerful. It has been used to some extent as a substitute for copaiba and oil of santal in the treatment of *cystitis* and *gonorrhea*. It has been frequently recommended as an *internal hemostatic* in hemorrhage from the uterus, lungs, intestines, and kidneys, especially when the bleeding is slight but persistent.

BUCHU, U. S. P.

Buchu is the leaves of *Barosma betulina*, growing in Southern Africa. Its active principle is a volatile oil.

PREPARATION

DOSE

Fluidextractum Buchu, U. S. P. $\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls).

Pharmacologic Action and Therapeutics.—In therapeutic doses buchu acts as a stimulant to the mucous membrane of the urinary tract. It is a feeble diuretic. The volatile oil is eliminated by the kidneys, and imparts to the urine an aromatic odor. Its presence also makes the urine more or less antiseptic. Overdoses may produce vomiting, purging, and strangury.

Buchu is useful in the less severe forms of *subacute and chronic cystitis*. It is especially efficacious in *chronic irritability of the bladder*, manifested by frequent desire to urinate. In *subacute cystitis* it may be advantageously combined with an alkali, as in the following formula:

R. Fluidextracti buchu f ʒvj (22.5 mls)
 Potassii citratis ʒss (15.0 gm.)
 Spiritus ætheris nitrosi f ʒj (30.0 mls)
 Syrupi limonis f ʒij (60.0 mls)
 Aquæ q. s. ad f ʒvj (180.0 mls).—M.

Sig.—A tablespoonful in water every three hours.

UVA URSI, U. S. P.

(Bearberry)

Uva ursi is the leaves of *Arctostaphylos Uva-ursi*, an evergreen shrub growing in the northern parts of Europe, Asia, and North America. It contains tannin and the glucosid, *arbutin*, which appears as white, crystalline needles, of a bitter taste, and freely soluble in alcohol or hot water, but sparingly soluble in cold water. The dose is from 2 to 5 grains (0.13–0.3 gm.).

PREPARATION

DOSE

Fluidextractum Uvæ Ursi, U. S. P. . . . $\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls).

Pharmacologic Action and Therapeutics.—*Uva ursi* in therapeutic doses stimulates the mucous membrane of the urinary

tract, increases the activity of the kidneys, and renders the urine slightly antiseptic. Arbutin is excreted by the kidneys partly unchanged and partly as hydroquinon. Both uva ursi and arbutin may impart to the urine a dark-green color, that is probably due to the presence of pigments derived from the oxidation of hydroquinon. As uva ursi contains a considerable quantity (6-8 per cent.) of tannin, it has well-marked astringent properties. For the same reason its preparations are incompatible with spirit of nitrous ether. Uva ursi may be employed to meet the same indications as buchu, but it is usually less efficient.

SABAL, U. S. P.

(Saw Palmetto Berries)

Sabal is the partially dried fruit of *Serenoa serrulata*, a palm growing in the Southern United States. Its activity is probably due to a volatile oil.

PREPARATION

DOSE

Fluidextractum Sabal, U. S. P. 15-30 min. (1.0-2.0 mls).

Sabal is used in the same class of cases as buchu and uva ursi.

CANTHARIS, U. S. P.

(Cantharides, Spanish Flies)

Cantharides (see p. 482) in moderate doses is an active stimulant to the mucous membrane of the urinary tract. In large doses it is a powerful irritant, causing intense abdominal pain, vomiting and purging, frequent micturition, dysuria, priapism, and scanty, albuminous, and, at times, bloody urine. The tincture, in doses of from 1 to 2 minims (0.06-0.1 mil), has been recommended in *chronic pyelitis*, *cystitis*, *urethritis*, and even the later stages of *parenchymatous nephritis*, but its use in these conditions is fraught with danger.

URIC-ACID SOLVENTS

Under this heading will be considered certain drugs that have been recommended to prevent the precipitation of insoluble urates in the body and to effect the solution of uratic concretions that have already been formed. The *alkalis* and *alkaline mineral waters* were among the first agents to be used for these purposes. That these remedies are sometimes beneficial in gout cannot be denied, but that they owe their efficacy to a solvent action on urates is highly improbable. Until we possess a more complete knowledge of the pathogenesis of gout, no adequate explanation

of the favorable action of the alkalis can be given. Doubtless much of the good that accrues to gouty patients from sojourns at watering-places is to be attributed to strict regimen, temperate living, agreeable exercise in the open air, and the liberal use of pure water, rather than to the specific action of any salts that may be contained in the waters.

It is possible by the administration of alkalis to keep uric acid in the urine from precipitating, by transforming it into more soluble acid urates, and, perhaps, to a slight extent, to redissolve uric-acid gravel. There is, however, no evidence that fully formed calculi in the renal pelvis or bladder or uratic tophi in the tissues can be redissolved by the administration of alkalis.

Knowing that *benzoic acid* was excreted in the urine chiefly as the soluble hippuric acid, Ure assumed that the drug would be efficacious as a uric-acid solvent in gout and nephrolithiasis. In consequence, the acid itself and its salts have been repeatedly recommended in these conditions. But the assumption is opposed to the results of more recent investigations, which have shown that the hippuric acid is formed in the kidney, and not in the blood, and, moreover, that its formation is not attended by a corresponding decrease in the excretion of uric acid.

Piperazin, or **diethylendiamin**, has been highly recommended for its solvent effects in gout and nephrolithiasis, but in the experience of many observers it has proved to be entirely inert. It is prepared by the action of ammonia on ethylene bromid or chlorid, and appears as colorless, acicular crystals, very hygroscopic, and freely soluble in water. Its dose is from 5 to 10 grains (0.3–0.65 gm.), well diluted. The only appreciable effect of such doses is a moderate increase in the quantity of urine. The excretion of uric acid, even in the presence of gouty concretions, is not increased. Large doses may cause nausea, malaise, stupor, muscular weakness, tremors, and incoördination. Solutions of 1 or 2 per cent. in normal urine will readily dissolve fragments of uric acid calculi in the test-tube, but the amount of unoxidized piperazin appearing in the urine after ordinary doses have been administered by the mouth has been shown to be without solvent action. Gouty tophi have been removed by the local injections of the drug, but the treatment is said to be very painful. *Lycetol*, or dimethylpiperazin tartrate, and *lysidin*, made by the interaction of ethylendiamin hydrochlorid and sodium acetate, are claimed to be more powerful solvents of uric acid than piperazin.

Tartrate of piperidin, which was introduced by Tunnicliffe and Rosenheim as a solvent of gouty concretions, is effective outside of the body, but clinically the results with it are questionable. Weiss, Fränkel, Ewald and others have advocated the

use of quinic acid in combination with lithium (urosin) or with piperazin (sidonal), but according to Denis, it neither decreases the urate content of the blood or increases urate elimination.

Cinchophen and the *salicylates* cause increased elimination of uric acid from the blood, and this effect is probably due to a lowering of the renal threshold for uric acid (Denis). *Cinchophen*, however, favors the precipitation of uric acid in the urine (Haskins) and, therefore, it should be avoided in uratic lithiasis.

APHRODISIACS AND ANAPHRODISIACS

Aphrodisiacs are agents that stimulate sexual appetite and promote virility. Sexual impotence results from a variety of causes; in consequence its treatment, to be successful, must vary accordingly. In one instance the symptom is due to diabetes mellitus, in another to locomotor ataxia, and in still another to neurasthenia. The last is the most common cause of acquired impotence, and its diverse etiology must be carefully considered in formulating any line of treatment. Hygienic measures, such as pertain to food, physical exercise, rest, clothing, etc., should never be neglected. Abstinence from all sexual excitement is essential. Iron and arsenic are indicated if there is anemia. Hydrotherapy and massage are often useful adjuvants to other measures. Electricity, locally applied, is sometimes beneficial. A large electrode—the positive—should be applied over the lumbar spine, while the negative electrode is applied over the spermatic cord or perineum. A current of from 5 to 10 milliamperes is sufficient. Hirt has repeatedly seen good effects follow the introduction of a metal-tipped sound into the urethra as far as the fossa navicularis, while the positive pole (anode) is placed over the lumbar cord, the current at the negative pole being made and broken several times. In many instances the psychic element is the all-important factor, and if such is the case, treatment must be directed to the mind rather than to the body. Advice intended to promote confidence, to give encouragement, and to distract the patient's thoughts from his infirmity will be the most effectual.

The chief drugs for which special aphrodisiac power has been claimed are:

Nux vomica
Phosphorus

Cantharides
Yohimbin

Testicular extract.

In certain cases of impotence *nux vomica* proves useful, not only through its general tonic influence, but also through its stimulant action on the sexual centers of the spinal cord.

Phosphorus has not the stimulating influence on the central nervous system that was formerly claimed for it; nevertheless, it seems to be of service in some cases of sexual neurasthenia. The drug may be prescribed as phosphorus in doses of from $\frac{1}{100}$ to $\frac{1}{50}$ grain (0.00064–0.0013 gm.), or as phosphid of zinc, in doses of from $\frac{1}{20}$ to $\frac{1}{10}$ grain (0.003–0.006 gm.).

Cantharides in large doses, by irritating the bladder and urethra, sometimes induces sexual emotions and erections, but in doses that can be regarded as safe the drug is entirely without aphrodisiac influence.

Yohimbin is an alkaloid or a mixture of alkaloids obtained from the bark of the Cameroon tree—Yohimbehe—growing in West Africa. According to Loewy it produces congestion of the testes and stimulates sexual appetite. The dose is from $\frac{1}{12}$ to $\frac{1}{6}$ grain (0.005–0.01 gm.). Berger and Eulenberg have employed the drug with asserted good results in sexual neurasthenia. Kravkoff, however, found that the congestion of the sexual organs is not due to any selective action, but to a general vasodilating effect, and that while the drug possesses no aphrodisiac influence, it is, in the dose recommended, distinctly toxic. Solutions of yohimbin, when instilled into the eye, dilate the pupil without impairing accommodation, and when applied to mucous membranes produce an anesthetic effect comparable to that of cocain.

Good results from the *transplantation of pieces of testicle* into the abdominal wall or into the scrotum have been claimed by Lydston and others in impotence due to insufficiency of the testicles, but the evidence is not wholly convincing. In Lydston's experiments the transplanted tissue entirely disappeared after 12 or 18 months. The administration of *testicular extracts* by the mouth has not proved beneficial.

Anaphrodisiacs are drugs that decrease sexual desire. The most important members of the group are:

Scopolamin (hyoscin)

Bromids

Camphor.

Anaphrodisiacs are useful in satyriasis, nymphomania, spermatorrhea, priapism, and chordee. Scopolamin and the bromids are the most reliable of all drugs for subduing morbid excitability of the genital organs. Camphor in itself is of little value, but the monobromated camphor is often efficacious.

Spermatorrhea and impotence are not infrequently associated symptoms in neurasthenia, and when such is the case, an anaphrodisiac, such as scopolamin, may be given at bedtime to overcome the irritable weakness of the sexual apparatus, while general roborant measures are employed to combat the nervous exhaustion. In some instances seminal incontinence is the result of a local cause, such as persistent constipation, hemorrhoids, prostatic hypertrophy, phimosis, extreme sensibility of the prostatic urethra, or loading of the urine with crystals of uric acid or calcium oxalate. It is needless to say that under these circumstances the removal of the local irritation is of paramount importance. Local applications of cold water, avoidance of stimulating food, sleeping on a hard mattress without too much covering, the adjustment of some mechanical device to prevent the patient from sleeping on his back, are measures that tend to lessen the sensitiveness of the genital organs. When the emissions occur toward morning and are excited by distention of the bladder, it is a good plan to have the patient form the habit of voiding his urine at 1 or 2 o'clock in the morning.

EMMENAGOGUES

Emmenagogues are remedies that promote the menstrual flow. They may act indirectly by removing the remote pathologic cause of amenorrhea, or they may act directly by stimulating the uterus itself. There are very few indications for the employment of direct emmenagogues. In a large class of cases the suppression of the menstrual flow is dependent upon some general cause which has resulted in constitutional enfeeblement; thus it may be due to anemia, persistent constipation, tuberculosis, nephritis, diabetes, extreme obesity, or myxedema. In such cases treatment should be directed to the primary disease, there being rarely any indication to address remedies to the amenorrhea as such. In conjunction with measures intended to improve the general nutrition, *iron* will be found efficacious in chlorosis, purgatives, especially *aloes*, if there is obstinate constipation, and *thyroid extract* if myxedema or hypothyroidism is the primary factor. *Ovarian extract* and *corpus luteum extract* are sometimes of service in amenorrhea due to disturbance of the endocrine glands. In some cases absence of menstruation is dependent upon a pronounced defect in the development of the genital organs or upon atresia of the genital passages. Under such circumstances, emmenagogues would, of course, be of no avail. Again, amenorrhea may be a symptom of uterine or ovarian disease, and if such is the case, it is manifestly improper to goad the affected organs

with stimulating drugs. Occasionally suppression is associated with some psychic disturbance, such as grief, anxiety, or fear. In these cases restoration of the catamenia usually occurs after a time without recourse to special medication. Acute suppression from exposure to cold should be treated by rest in bed, hot sitz-baths, hot drinks, and hot applications to the abdomen and genitals. Constipation should be relieved by a laxative dose of aloes, and febrile reaction controlled with such remedies as aconite or acetphenetidin.

The only indications for treating amenorrhea as such by the use of direct uterine stimulants are: (1) When the suppression itself is the cause of painful symptoms—that is, when there is a menstrual colic without bloody discharge; (2) when the menses do not return upon the restoration of the general health, as is sometimes the case in girls during the developmental period.

In pregnant women emmenagogues in large doses act as ecbolics or abortifacients.

Of the many drugs that have been used as direct emmenagogues probably the most reliable are two preparations of manganese—*potassium permanganate* and *manganese dioxid*. A number of other drugs that tend to induce uterine congestion by irritating the intestines or the urinary tract have also popular reputation as emmenagogues. In this group are *apiol*, *senecio*, *myrrh*, *pennyroyal*, *tansy* and *savin*. Cantharis and oxalic acid produce a similar effect, but their use as emmenagogues is fortunately obsolete.

Manganum (Manganese, Mn).—The finding of traces of manganese in the red-blood cells and other tissues led to the recommendation of its compounds in the treatment of chlorosis and other forms of anemia, but in the judgment of competent observers the drug is valueless as a hematinic. Ringer was the first to recommend potassium permanganate as an emmenagogue, and there is sufficient evidence at present to establish its worth in this respect. It probably acts directly on the uterus, and not indirectly, through any influence exerted on the blood. It is most efficacious when given a few days before the expected menstrual period. It should be prescribed in doses of from 1 to 3 grains (0.065–0.2 gm.), in pills made with kaolin or soft paraffin, and these should be taken after meals in large drafts of water. As potassium permanganate is a highly irritating salt, and, moreover, as it is at once decomposed in the stomach into the black oxid of manganese, the latter preparation (*Mangani Dioxidum Præcipitatum*, U. S. P.), which is free from irritant properties, may be substituted with advantage. Its dose is from 2 to 5 grains (0.1–0.3 gm.).

Apiol is an oleoresin obtained from *Apium Petroselinum*, or garden parsley. It is a greenish oily liquid from which a crystalline stearopten is obtained, known as *white apiol*. The dose of apiol is from 3 to 8 minims (0.18–0.5 mil), in capsules. When given for a few days before the expected period it is a fairly reliable emmenagogue.

Senecio (*Ragwort*) is the entire plant of *Senecio aureus*, a perennial herb growing in the northern and western parts of the United States. In the form of a fluidextract or tincture it has been highly recommended as a corrective of *functional amenorrhea and dysmenorrhea*. The dose of the fluidextract is from $\frac{1}{2}$ to 1 fluidram (2.0–4.0 mils).

Myrrha, U. S. P. (*Myrrh*), is a gum-resin obtained from *Commiphora Myrrha*, a small tree growing in eastern Africa and Arabia. It appears in the form of brownish-red irregular-shaped tears, having an agreeable aromatic odor and a bitter acrid taste.

PREPARATIONS

DOSE

Tinctura Myrrhæ, U. S. P.	10–30 min. (0.6–2.0 mils)
Pilulæ Rhei Compositæ, U. S. P. (aloes, $1\frac{1}{2}$ gr.— 0.1 gm.; rhubarb, 2 gr.—0.13 gm.; myrrh, 1 gr.— —0.06 gm.)	1–5 pills.

Myrrh is used as an emmenagogue and as a stimulant to mucous membranes. When employed as an emmenagogue, it is usually associated with iron or aloes. The tincture, diluted with water, or with a weak solution of borax or potassium chlorate has been extensively employed as a local application in *mercurial ptyalism, ulcerative stomatitis, and spongy gums*.

R. Potassii chloratis	gr. xl (2.6 gm.)
Tincturæ myrrhæ	f 3iss (45.0 mils)
Tincturæ benzoinæ compositæ	f 3vj (23.0 mils)
Liquoris antiseptici	q. s. ad f 3iv (118.0 mils).—M.

SIG.—Teaspoonful in a wineglassful of water as a mouth-wash every two hours.

Myrrh was also used at one time as a stimulant expectorant in *chronic bronchitis*, but it has been replaced by more efficient remedies.

Pennyroyal is the leaves and tops of *Hedeoma pulegioides*, an annual herb indigenous to North America. It contains a volatile oil, a bitter principle and tannin. In the form of a hot infusion (1–2 fl. oz.—30.0–60.0 mils) it has a popular reputation as an emmenagogue, which is not altogether unmerited. It is especially employed in acute suppression of the menses brought on by exposure to cold.

Tansy is the leaves and tops of *Tanacetum vulgare*, a perennial herb growing wild in Europe and Asia, and naturalized in North

America. Its active principle is a volatile oil, the dose of which is from 1 to 5 minims (0.06–0.3 mil). Tansy has been used as a domestic remedy in *amenorrhea*, the herb itself being usually given in doses of from $\frac{1}{2}$ to 1 dram (2.0–4.0 gm.) in decoction. The oil has been used somewhat extensively as an abortifacient, many times with ill success, but with grave or even fatal results to the mother. Large doses of the oil cause abdominal pain, vomiting, epileptiform convulsions, coma and collapse.

Savin is the tops of *Juniperus Sabina*, an evergreen shrub growing in Northern Europe, Asia, and America. Its active constituent is a volatile oil, the dose of which is 3 to 5 minims (0.2–0.3 mil). Oil of savin has an action resembling that of oil of juniper, but it is more irritant and toxic. Large doses cause abdominal pain, vomiting, purging, anuria, unconsciousness, and collapse. In pregnant women the intoxication generally culminates in abortion. Owing to the fact that expulsion of the fetus does not occur until the irritation of the intestinal canal and kidneys is sufficiently violent to endanger life, many cases of fatal poisoning have resulted from the use of the drug as an abortifacient. Oil of savin has been used in *amenorrhea*, but at the present time is very rarely prescribed.

OXYTOCICS, OR ECBOLICS

Oxytocics are drugs that accelerate parturition by strengthening the uterine contractions. It is not definitely known how some of them produce their results. The abortifacient action of certain drastic purgatives, such as aloes, and of certain volatile oils, such as oil of tansy and oil of savin, seems to be the result of a *reflex stimulation of the uterus through irritation of the intestine*. Other drugs, such as ergot, pituitary extract, and probably quinin produce their ecboic effect by *directly stimulating the uterine muscle itself*. Epinephrin augments contractions in the gravid uterus by stimulating the sympathetic (hypogastric) nerve-endings, but its action on the uterus is ephemeral and subordinate to that on the bloodvessels. The important oxytocics are:

Ergot
Pituitary extract
Quinin.

Corn smut, cotton-root bark and hydrastis also have a stimulating effect upon the uterus, but are unreliable.

Indications.—Oxytocics may be employed during labor to hasten the expulsion of the fetus; at the close of labor, to prevent

or to check postpartum hemorrhage; and in the puerperium to overcome certain forms of subinvolution.

ERGOTA, U. S. P.

(Ergot, Ergot of Rye, *Secale Cornutum*)

Ergot is a parasitic fungus, *Claviceps purpurea*, growing on the grain of common rye, *Secale cereale* and more rarely other grains.

It is obtained chiefly from Russia, Germany and Spain. The official ergot* is in triangular, slightly curved pieces from $\frac{1}{2}$ to 1 inch (20–25 mm.) long and from $\frac{1}{8}$ to $\frac{1}{4}$ inch (3–6 mm.) in diameter. Externally, it is purplish-black, and internally, whitish with pinkish striæ. It has a peculiar heavy odor and an unpleasant oily taste. It deteriorates on keeping and is said to be unfit for use when more than a year old. The average dose of ergot is 30 grains (2.0 gm.).

Ergot contains a number of principles, of which the most important are the alkaloid, ergotoxin, two ptomain-like bases tyramin and histamin, and a derivative of cholin, acetyl cholin.

Ergotoxin, except in massive doses, powerfully stimulates smooth muscle, in particular that of the arterioles and uterus, and is, therefore, a vasoconstrictor and ecboic. Strong concentrations paralyze augmentary sympathetic endings. Ergotoxin is insoluble in water and consequently is not present in aqueous extracts of ergot.

Histamin is present in extracts of all animal tissues and both histamin and tyramin occur in putrid meat. Histamin, administered parenterally, stimulates smooth muscle, even in small doses, and is a powerful ecboic. It has but little effect, however, when administered by the mouth, as it is destroyed before it is absorbed.

Tyramin, when administered intravenously or subcutaneously, is an energetic vasoconstrictor, producing this effect, probably, like epinephrin, by stimulating the sympathetic nerves. It has little influence on the vessels when administered by the mouth.

Acetyl cholin has an inhibitory action on the heart and a stimulant action on the intestinal muscle.

Less important constituents of ergot are the alkaloid, ergotinin and the sapotoxin, ergotinic acid. *Ergotinin* itself is almost inactive, but it is readily converted into ergotoxin by hydration; *ergotinic acid*, like other sapotoxins, is locally irritant, but is not absorbed from the digestive tract.

PREPARATIONS

DOSE

Fluidextractum Ergotæ, U. S. P. . . . $\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mils)
Extractum Ergotæ, U. S. P. 3–10 gr. (0.2–0.6 gm.).

* The word is from the French, ergot, a cock's spur.

Several purified extracts of ergot are available for hypodermic use and may be given in doses of 3 to 8 grains (0.2–0.5 gm.). The isolated principles of ergot are rarely used for clinical purposes. Ergotoxin is employed in the laboratory to paralyze vasoconstrictor and other sympathetic nerve-endings.

Pharmacologic Action.—Ergot, when injected intravenously, in large doses, causes a primary fall of the arterial pressure, followed by a rise, which is more prolonged but much less pronounced than that produced by epinephrin or pituitary extract. The primary fall of pressure is probably due to depression of the heart by the acetyl cholin, while the secondary rise is due to peripheral vasoconstriction by the ergotoxin (stimulation of the arterial muscle) and the tyramin (sympathetic stimulation). Taken by the mouth in single large doses ergot is without effect upon the arterial pressure. Taken over long periods, however, it is capable of producing gangrene in distal parts of the body, such as the toes, fingers and nose. The gangrene is usually ascribed to prolonged constriction of the arterioles, but it is probably due to occlusion of the vessels by hyaline thrombi, produced by a toxic effect of the drug on the vascular endothelium. Certain animals, such as the rooster and the pig, are particularly susceptible to the gangrene action of ergot. In roosters the drug produces cyanosis and coldness of the comb and wattles in an hour or two, and if it is given repeatedly, these appendages become gangrenous and fall off. Gangrene has also been frequently observed in human beings suffering from chronic ergot-poisoning.

Nervous System.—Ordinary doses of ergot, if not long continued, have no appreciable influence on the nervous system. In acute poisoning, however, epileptiform convulsions occur and are probably due to stimulation of the medulla. In one form of chronic poisoning nervous phenomena are also pronounced, and are probably due to circulatory disturbances in the central nervous system, or, if permanent, to degenerative changes of vascular origin. The chief phenomena are paresthesia, anesthesia, tonic spasms of the muscles, ataxia, mental dulness and dementia.

Alimentary Canal.—Large doses of ergot frequently excite nausea or vomiting. This effect seems to be due in part to the local irritant action of the drug and in part to stimulation of the vomiting center. Injections of ergotoxin increase the peristaltic movements, both of the stomach and intestine.

Uterus.—In the parturient woman moderate doses of ergot induce uterine contractions which often closely resemble the rhythmic contractions observed in normal labor. After large doses, however, the contractions usually become very power-

ful and uninterrupted or tetanic. The preparations of the drug on the market vary so much in activity that it is difficult to predict the effect of an average dose in a given case. The influence of ergot on the gravid but non-parturient uterus is much less marked, and it is doubtful whether the drug, except in poisonous doses, is capable of originating expulsive movements that culminate in abortion. The ecboic effect of ergot depends chiefly upon ergotoxin and histamin, and is apparently due to direct stimulation of the uterine muscle.

Toxicology.—*Acute ergotism* is characterized by symptoms of gastro-enteritis—abdominal pain, nausea, vomiting and diarrhea and various nervous phenomena, such as headache, vertigo, paresthesias, epileptiform convulsions, delirium, stupor and coma. In pregnant women abortion usually occurs. Death is due to circulatory failure.

Chronic ergotism assumes two types: the spasmodic and the gangrenous. In both types the early symptoms usually consist of gastrointestinal derangements, debility, headache, dizziness, disturbance of vision, and various paresthesias, particularly formication. Later, in the spasmodic type muscular twitchings develop, especially in the extremities, and pass into tonic and clonic spasms and sometimes into permanent contractures. General epileptiform seizures and psychic disturbances, mimicking various forms of insanity, may also occur. Ultimately, the symptom-complex may resemble more or less closely that of tabes dorsalis. In the gangrenous type the gastrointestinal disturbances and paresthesias are followed by sloughing of the tissues in certain parts of the body, especially the fingers, toes, ears and nose.

Therapeutics.—Because of the uncertainty of its effect and the possibility of its causing continuous or tonic contractions of the uterus, ergot should not be employed in *labor* until after the uterus has been emptied. Its use in effective doses, especially if dystochia is due to contracted pelvis, rigid cervix, displacement of the uterus, abnormal presentation, or other physical abnormality, may result in asphyxiation of the fetus or even rupture of the uterus. At the close of labor, after the uterus has been emptied, it is effective in preventing or controlling *postpartum hemorrhage*. It is sometimes of service also in overcoming *subinvolution of the uterus*. Ergot has been employed somewhat extensively in the treatment of *uterine fibroids*, but it is of little value, except in controlling temporarily the bleeding. The drug is sometimes useful in *metrorrhagia* and *menorrhagia* from various causes, but there is no satisfactory evidence that it is of value in other forms of hemorrhage, such as hemoptysis, hematuria, and hema-

temesis. Ergot is said to have been used with some success in *diabetes insipidus* (Da Costa, Ringer) and in *headache of migrainous type* (Thomson). The drug has also been highly recommended in *delirium tremens*, especially when meningitic symptoms ("wet brain") are prominent.

Administration.—The preparations of ergot on the market vary considerably in strength. The best preparation for administration by the mouth is a good assayed fluidextract. Its effects on the uterus are usually apparent in from 20 minutes to half an hour. In urgent cases, as in postpartum hemorrhage, the drug is best given hypodermically. The injections should be made into a muscle and not directly beneath the skin. Sterile glass ampoules containing purified extracts of ergot are available for the purpose.

OTHER OXYTOCICS

Pituitary Extract (see p. 63).—Intravenous, intramuscular and subcutaneous injections of pituitary extract (posterior lobe) have a powerful stimulating effect upon the uterus, especially in labor. The action of the drug, like that of ergot, is on the uterine muscle, but it is more prompt and powerful than that of ergot, although it is less persistent. Large doses cause tetanic contractions of the uterine muscle.

As an oxytocic, pituitary extract should be employed only when the cervix is fully dilated and delay in delivery is due solely to *uterine inertia*. Instances of premature separation of the placenta, asphyxia of the fetus, laceration of the cervix, etc. following its use have been reported somewhat frequently. The dose is $\frac{1}{2}$ c.c. ($\frac{1}{2}$ mil), intramuscularly, repeated in an hour, if necessary. Because of its very prompt action, pituitary extract is a valuable remedy in *postpartum hemorrhage*, but it is advisable to follow its use with that of ergot, as the effect of the latter is more persistent.

Quinin (see p. 446).—This drug has some power of increasing the rapidity and energy of the uterine contractions when they have once begun; its action, however, is inconstant. The contractions are much less prolonged than those excited by ergot, and are probably due to an influence exerted directly on the uterine muscle. As the drug does not seem capable of originating labor-pains, it cannot be considered an active ecboic, and the cases of abortion that have been reported as following its administration have no doubt been due either to an idiosyncrasy or to the original disease for which the quinin was prescribed. According to some obstetricians, its use during labor distinctly increases the tendency to postpartum hemorrhage.

Hydrastis (see p. 197).—Both the natural alkaloid of this drug, *hydrastin*, and its artificial derivative, *hydrastinin*, have an action on the uterus similar to that of ergot, but less powerful. For its effect on the uterus hydrastinin is preferable to hydrastin. Hydrastinin has been used with more or less success in *menorrhagia* and *metrorrhagia* from various causes, and also in *subinvolution* of the uterus. In postpartum hemorrhage is much less reliable than ergot or pituitary extract.

Cotton-root Bark.—This drug (*Gossypii Cortex*) is said to have been much valued by the slaves in southern states as an abortifacient. Some obstetricians have claimed for it an action resembling that of ergot. The dose of the fluidextract as an ecboic is from $\frac{1}{2}$ to 2 fluidrams (2.0–8.0 mils).

Corn Smut.—This drug (*Ustilago Maydis*) is a fungus growing on the stems and tassels of *Zea Mays*, or Indian corn. According to some obstetricians, the fluidextract, in doses of $\frac{1}{2}$ to 1 fluidram (2.0–4.0 mils), induces in the parturient uterus vigorous but intermittent contractions, and is, therefore, a useful stimulant when the labor pains are feeble from exhaustion.

DIAPHORETICS, OR SUDORIFICS

Diaphoretics are agents that promote the secretion of sweat. They may act by stimulating the terminations of the secretory nerves, by stimulating the sweating center, by dilating the blood-vessels of the skin, or, reflexly, by irritating peripheral sensory nerves. The activity of the sweat-glands may also be increased by external heat, muscular exercise, dyspnea, strong emotion, and nausea.

Although dilatation of the cutaneous vessels promotes perspiration when other conditions are not unfavorable, the mechanism of sweat secretion is in large measure independent of the blood-flow. Thus, in fever the flushed skin may be unnaturally dry, while in collapse, with pallid skin, there may be free perspiration. External heat may act partly by inducing hyperemia of the skin, but that it acts chiefly by stimulating the sweat-fibers reflexly through the cutaneous sensory nerves appears evident from the fact that exposure of a part to a high temperature does not cause sweating if all the nerves leading to the part be severed. Muscular exercise probably acts by increasing the flow of blood to the glands and by stimulating the peripheral nerves and the nerve-centers. Dyspnea acts by increasing the proportion of venous blood, the latter being a powerful stimulant of the sweat-centers. Strong emotions affect secretion probably

also by action on the nerve-centers. The sweating that attends nausea is, no doubt, induced reflexly by stimulation of the sweat-centers through the sensory nerves of the stomach. Among drugs, pilocarpin owes its diaphoretic effect to stimulation of the nerve-endings in the gland-cells, while alcohol and opium favor sweating, probably by dilating the skin vessels. The drugs most commonly employed as diaphoretics are:

Pilocarpus (pilocarpin)	Spirit of nitrous ether
Opium	Ammonium acetate
Ipecacuanha	Warburg's tincture.

The use of *external heat* is also a valuable means of inducing diaphoresis. It may be applied in the form of the Turkish bath (dry heat), Russian bath (moist heat), hot pack, hot-air bath, vapor bath or electric bath.

Indications.—Diaphoretics are used (1) to promote the absorption of dropsical effusions; (2) to remove excrementitious material from the blood, and thus relieve the kidneys; and, (3) by increasing the vascularity of the skin, to arrest the development of local congestions and inflammations, especially when these have resulted from chilling of the body.

PILOCARPUS, U. S. P.

(Jaborandi)

Pilocarpus is the dried leaflets of *Pilocarpus Jaborandi* or *Pilocarpus microphyllus*, shrubs growing in Brazil. It contains three alkaloids: *pilocarpin*, *pilocarpidin* and *isopilocarpin*, which produce similar effects, but pilocarpin is the most active, and is present in larger quantity ($\frac{1}{4}$ – $\frac{1}{2}$ per cent.) than the others.

Pilocarpin yields soluble crystalline salts, of which the nitrate (Pilocarpinæ Nitras, U. S. P.) and the hydrochlorid (Pilocarpinæ Hydrochloridum, U. S. P.) are usually employed. The dose of either of these salts is from $\frac{1}{12}$ to $\frac{1}{4}$ grain (0.005–0.015 gm.).

PREPARATION

DOSE

Fluidextractum Pilocarpi, U. S. P.. 20–60 min. (1.2–4.0 mls).

Pharmacologic Action.—Pilocarpin stimulates the ends of the nerves belonging to the parasympathetic division of the “vegetative” or autonomic nervous system—oculomotor, vagus, and secretory nerves.* Its action is similar in many respects to that of physostigmin, and, in its peripheral effects, antagonistic to that of atropin.

* The innervation of the sweat-glands, although it is anatomically sympathetic, reacts pharmacologically as if it were parasympathetic.

Secretions.—The dominant action of pilocarpin is stimulation of the nerve-endings in the secretory glands. The diaphoretic effect of the drug is especially pronounced, $\frac{1}{4}$ grain (0.015 gm.) hypodermically, under favorable conditions, causing profuse perspiration lasting an hour or two. Accompanying the diaphoresis, there is usually more or less hyperemia of the skin. Pilocarpin also increases, but to a less extent, the saliva, the tears, the mucous secretions and the gastric, intestinal and pancreatic juices. It has no direct effect on the secretion of bile or urine, and very little on that of milk, the functions of the liver, kidneys and mammary glands being in large measure free of nervous control. By stimulating the secretions of the scalp it favors the growth of hair.

The Eye.—The actions of pilocarpin on the eye are similar to those of physostigmin, but less powerful. Like physostigmin, it produces when used locally miosis, spasm of accommodation, and a decrease of intraocular tension.

Muscles.—By acting directly on the nerve-endings, pilocarpin excites contractions in the smooth muscle of the stomach, intestines, bronchi, uterus, bladder and spleen, but not in that of the arterioles. Its action in this respect is less pronounced than that of physostigmin. The drug has no action on striped muscle.

Circulatory System.—Large doses of pilocarpin first stimulate and then depress the vagus peripherally, the result being transitory slowing of the pulse, followed by marked quickening. Toxic doses also lower the bloodpressure by depressing the heart itself and the vasoconstrictor center. When the heart is weak even therapeutic doses may cause serious collapse.

Respiration.—Small doses have no direct effect; toxic doses depress the respiratory center. Occasionally, even therapeutic doses cause considerable dyspnea by flooding the bronchi with mucus. In poisoning by pilocarpin depression of the circulation may result in true pulmonary edema.

Alimentary Canal.—Pilocarpin stimulates the gastric and pancreatic secretions and increases the gastric and intestinal movements. From a therapeutic viewpoint, however, these actions are unimportant, as they are entirely overshadowed by the drug's diaphoretic action. In pilocarpin-poisoning vomiting, diarrhea and colic may be conspicuous features. They have been ascribed to the stimulant effects of the drug on the stomach and bowel, but, according to Eggleston and Hatcher, the vomiting is mainly of central origin.

Actions of Pilocarpin and Physostigmin Compared.—While the peripheral actions of pilocarpin and physostigmin

agree qualitatively, they differ quantitatively. Thus, the action of physostigmin on smooth muscle is somewhat stronger than that of pilocarpin, but its action on secretions is much weaker. Pilocarpin is less depressing to the central nervous system than physostigmin and lacks entirely the stimulating action of the latter on the nerve-endings in the skeletal muscles.

Toxicology.—The chief phenomena of pilocarpin-poisoning are profuse sweating, salivation, nausea and vomiting, diarrhea, intestinal cramps, miosis, muscular tremors, dyspnea, and collapse. Atropin is an effective physiologic antidote. Hot applications and stimulants are required to combat collapse.

Idiosyncrasies and Untoward Effects.—The action of pilocarpin in man is by no means constant. Occasionally, even moderate doses are followed by severe cardiac depression or a condition simulating pulmonary edema. Swelling of the salivary glands, profuse salivation, persistent nausea and vomiting, and strangury have also been observed after its administration. On the other hand, there may be a peculiar insusceptibility to its action, as in a case reported by Hare, in which a woman of 30 years received $\frac{3}{4}$ grain (0.05 gm.) of pilocarpin hydrochlorid in half an hour without any effect.

Therapeutics.—Pilocarpin in doses of from $\frac{1}{16}$ to $\frac{1}{12}$ grain (0.004–0.005 gm.) is often useful in promoting moderate diaphoresis in *acute and chronic parenchymatous nephritis*. It tends to avert uremia by relieving the congestion of the kidneys and by ridding the blood of poisonous matters. Its action should be supplemented by external heat. The remedy may be repeated every other day or even every day. In *acute uremia* larger doses, $\frac{1}{8}$ to $\frac{1}{4}$ of a grain (0.008–0.015 gm.), may be employed in conjunction with hot-air or vapor baths. In *puerperal eclampsia* the drug is often badly borne. In *general dropsy*, due to Bright's disease, pilocarpin may be a valuable aid to absorption. In local effusions, however, such as occur in the pleura and pericardium, it is not effective. It is sometimes employed for its diaphoretic effect in *myalgia*, *acute coryza*, and *acute sthenic infections*.

Daily injections of pilocarpin ($\frac{1}{6}$ gr.—0.01 gm.), as first employed by Politzer in 1880, have given gratifying results in some forms of *acute and subacute labyrinthine disease*, characterized by deafness, tinnitus aurium, and vertigo.

In the eye pilocarpin has been used to lessen intraocular tension in *glaucoma*, but physostigmin is more reliable. When, however, a gentle but persistent stimulant effect on the ciliary muscle is desirable, as in cases of *accommodative asthenopia*, pilocarpin will be found serviceable. As an adjuvant to mixed

treatment, daily injections of pilocarpin have sometimes proved efficacious in intractable cases of *syphilitic keratitis*. They have been found efficacious also in *opacities of the vitreous humor*. There is some evidence to prove that the internal administration of pilocarpin promotes the growth of hair, and at the same time renders it darker and coarser. Favorable results from the hypodermic use of the drug in *extensive alopecia* and *alopecia areata* have been reported by Simon, Pick, Morris, Pringle, and others, but the practice of applying the remedy in the form of lotions to the scalp in premature baldness is of doubtful utility.

Contraindications.—If the heart is weak or if any pulmonary disease is present pilocarpin should be avoided. Caution should be exercised also in giving the drug to women advanced in pregnancy, as it possesses some power as an abortifacient.

Administration.—On account of the uncertain alkaloidal strength of the fluidextract, one of the salts of pilocarpin is always preferable. The latter may be given by the mouth, but when a prompt or pronounced effect is desired, it should be given hypodermically. Its diaphoretic action is greatly facilitated by external heat. Circulatory depression should be combated with ammonia, camphor, or strychnin, and pulmonary edema with hypodermic injections of atropin. According to Tyson, a freshly prepared infusion may be injected into the rectum with prompt results. Four ounces (120.0 mls) of hot water should be poured on a dram (4.0 gm.) of jaborandi leaves, and, when sufficiently cool, strained and injected.

OTHER DIAPHORETICS

Opium (see p. 86).—As a diaphoretic, opium is employed in the form of Dover's powder, or powder of ipecac and opium. This preparation, in doses of from 5 to 10 grains (0.3–0.6 gm.), produces a mild sudorific effect, and is useful in the early stages of *acute catarrhal conditions of the respiratory organs*, *acute amenorrhea from chilling of the body*, and in *acute myalgia*. It should be borne in mind that large doses not infrequently cause nausea or even vomiting when the stomach is sensitive.

Spirit of Nitrous Ether (see p. 252).—Sweet spirit of niter (Spiritus Ætheris Nitrosi, U. S. P.) is an alcoholic solution of ethyl nitrite, yielding, when freshly prepared, not less than eleven times its own volume of nitrogen dioxid, the equivalent of about 4 per cent. of pure ethyl nitrite. It is a clear, volatile, inflammable liquid, having a pale yellowish or greenish-yellow tint, a pleasant ethereal odor, and a sharp, burning taste. On exposure to light and air it rapidly deteriorates. The dose for

an adult is from $\frac{1}{2}$ to 1 fluidram (2.0–4.0 mls); for a child, 15 to 30 minims (1.0–2.0 mls).

In medicinal doses nitrous ether acts as a mild diaphoretic, diuretic, and antispasmodic. When the patient is kept well covered after its administration, its diaphoretic effect is more pronounced than its diuretic effect, and the reverse is true when the patient is lightly covered. Toxic doses produce symptoms resembling poisoning by amyl nitrite and other nitrites. Sweet spirit of niter is a useful remedy in the *mild febrile affections of children*; it is best given in small doses, well diluted with hot water, at frequent intervals. As a diuretic it is sometimes efficacious in relieving *oliguria* due to *fever* or *acute congestion of the kidneys*. It is often given in conjunction with potassium citrate and ammonium acetate.

INCOMPATIBLES.—Iodids, tannin, antipyrin, mucilage of acacia.

Ammonium Acetate.—This compound is employed in the form of its official solution, the spirit of Mindererus (Liquor Ammonii Acetatis U. S. P.). According as the patient is kept warm or cool it is a very feeble diaphoretic or diuretic. It is often used in *febrile diseases* as a vehicle for spirit of nitrous ether or aconite. Its dose is from 1 to 4 fluidrams (4.0 to 15.0 mls).

Warburg's Tincture (see p. 454).—This preparation in doses of $\frac{1}{2}$ fluidounce (15.0 mls) is capable of inducing copious sweating. To be effective, it should be given undiluted, and drinks should be withheld. It has been commended in the *malignant types of malarial fever*.

ANTIHYDROTICS

Antihydrotics are agents that check the secretion of sweat. Theoretically, they may act by lessening the irritability of the sweat-centers; by depressing the terminal fibers of the secreting nerves, or, possibly, the secretory gland-cells themselves; or by stimulating the respiratory center. Brunton was the first to direct attention to the close relation existing between respiratory depression and the occurrence of colliquative sweats. When the respiratory center is exhausted from any cause it responds less readily than the sweat-centers to the stimulating influence of venous blood, in consequence of which profuse sweating results. This teaching accords with the well-known fact that respiratory stimulants are frequently efficacious in controlling the night-sweats of pulmonary tuberculosis. The most important antihydrotics are:

Atropin
Agaricin

Picrotoxin
Camphoric acid.

Sulphuric acid, *gallic acid* and *ergot* have also been employed, but they are of no value. In addition to internal remedies, certain external applications are useful in controlling excessive perspiration; thus, sponging the surface with *vinegar* and water or a hydro-alcoholic solution of *tannin* or *alum* sometimes affords relief. A weak solution of *formaldehyd*, as recommended by Hirschfeld, is an energetic antihydrotic, but its irritant effects on the eyes and respiratory tract forbid its use when the sweating is general. The night-sweats of advanced pulmonary tuberculosis may be controlled in the majority of cases simply by placing the patient under good hygienic conditions, with an abundance of fresh air, complete rest and regulation of the diet.

In local hyperidrosis internal remedies are not often effective. The best results are obtained from external applications, such as dusting powders containing salicylic acid, boric acid, or tannoform (a condensation product of tannin and formaldehyd), or lotions containing alcohol, tannin, or formaldehyd.

Atropin (see p. 73).—This is the most powerful of the antihydrotics. It checks the secretion of the sweat-glands by depressing the endings of the secretory (sympathetic) nerves. In doses of from $\frac{1}{200}$ to $\frac{1}{100}$ grain (0.0003–0.00064 gm.) at bedtime it often effectually controls the profuse *night-sweats of pulmonary tuberculosis*; unfortunately, however, its repeated use almost always results in untoward symptoms, such as dryness of the throat, thirst, dimness of vision, etc. The tincture of belladonna is sometimes employed as a lotion in *local hyperidrosis* occurring about the hands and feet, but it is of doubtful value.

Agaricin.—This is an extract from *Polyporus officinalis*, a fungus growing on the larch tree. The fungus itself (white agaric or purging agaric), although an active irritant, was recommended for excessive sweating by de Haen as early as 1768. Agaricin is an impure form of *agaric acid*, which appears as a white, odorless, almost tasteless powder, slightly soluble in water. The dose of agaricin is from $\frac{1}{4}$ to 1 grain (0.016–0.065 gm.) and of agaric acid, $\frac{1}{8}$ to $\frac{1}{4}$ grain (0.008–0.016 gm.) in capsule, pill or powder. Like atropin, the drug arrests the secretion of sweat by depressing the nerve-endings in the secretory glands. Large doses not rarely cause nausea and diarrhea. Agaric acid is less irritant and more reliable than agaricin.

Picrotoxin.—This is a neutral principle obtained from fish berries—*Anamirta cocculus* and *Anamirta paniculata*, growing in India and the Malayan Islands. It is a colorless, shiny,

crystalline powder of an intensely bitter taste. It is soluble in alcohol and in acidulous solutions, but only slightly so in water. The dose is from $\frac{1}{80}$ to $\frac{1}{50}$ grain (0.0008–0.0013 gm.).

The dominant action of picrotoxin is on the centers in the medulla, which it first stimulates and then paralyzes. Toxic doses produce violent epileptiform convulsions, rapid breathing, slowing of the pulse, elevation of bloodpressure, and vomiting, and finally, unconsciousness, collapse and death by asphyxia. The drug has been recommended for a number of conditions, but chiefly for controlling the *night-sweats of pulmonary tuberculosis*. It sometimes succeeds after atropin and camphoric acid have failed. It is best given by the mouth, at bedtime, in the form of a pill or tablet.

Camphoric Acid.—This is a crystalline powder made by oxidizing camphor with nitric acid. It is odorless, of a slightly acid taste, soluble in 160 parts of water, and readily soluble in alcohol. The dose is from 20 to 30 grains (1.3–2.0 gm.) in capsules or cachets or in an elixir. The drug is sometimes of service in controlling the *night-sweats of pulmonary tuberculosis*. It has a tendency, however, to excite nausea. Its antihydrotic effect has been ascribed to stimulation of the respiratory center (Kobert, Roth). Camphoric acid is best given about 2 hours before the time at which the sweating is likely to occur and repeated, if necessary, in 3 hours.

EXPECTORANTS

Expectorants are drugs that modify the secretion of the air passages and facilitate its expulsion. The exact manner of their action is not clear. Those that promote secretion and render it less viscid in character, and, therefore, more easy of removal, are usually termed *sedative expectorants*. Most of the latter are also emetics, and, no doubt, owe their power of increasing secretion very largely to their nauseating properties. As a rule, they are employed as expectorants in much smaller doses than are required to produce vomiting, but occasionally vomiting itself renders valuable service in expelling mechanically excessive accumulations of tenacious mucus from the bronchi. The increased secretion which these drugs induce may be of service in depleting the congested bronchi, in protecting their surfaces from the air, in diluting and washing out the irritant, and, possibly, in exercising a bactericidal influence. The sedative expectorants in common use are:

Salts of ammonium (chlorid and carbonate)	Apomorphin
Organic salts of potassium	Lobelia
Antimony (tartar emetic)	Quebracho
Ipecacuanha	Sanguinaria.
Squill	

Sedative expectorants are indicated in *bronchitis* when the expectoration is scanty and viscid, and the cough is frequent and harassing.

Drugs that stimulate the mucous membrane of the respiratory tract and lessen the quantity of sputum are known as *stimulant expectorants*. Some of them appear to act by imparting tone to the relaxed mucous membrane, and others also by exercising an antiseptic influence. The most important stimulant expectorants are:

Oil of turpentine (Terebene; Terpin hydrate)	Benzoin
Oil of eucalyptus	Balsam of Peru
Oil of myrtle (Myrtol)	Balsam of Tolu
Oil of sandalwood	Tar
Oil of cubeb	Creosote (Guaiacol)
Copaiba	Grindelia.

Stimulant expectorants are indicated in *bronchitis* when the expectoration is mucopurulent or purulent.

Adjuvants to Expectorants.—When cough is disproportionate to expectoration and is in itself a source of distress, drugs may be combined with expectorants that lessen the irritability of the cough center or of the afferent nerve-endings in the respiratory passages. The most reliable drugs for this purpose are *opium* (*morphin*, *codein*, *heroin*), *dilute hydrocyanic acid*, *chloroform*, *bromids* and *hyoscyamus*. Sometimes cough is dependent to a great extent upon excessive irritability of the fauces; if this be the case, demulcents—*licorice*, *glycerin*, *acacia*—will be found useful adjuvants. When the respiratory center has become weakened through persistent cough, *strychnin* will prove beneficial. When bronchial catarrh is accompanied by asthma, antispasmodics—*belladonna*, *Hoffmann's anodyne*, *chloroform*, *bromids*—may be associated with expectorants. *Lobelia* is particularly useful in these cases, because it is both an expectorant and a depressomotor. Not rarely bronchial catarrh is kept up by venous congestion of the lungs, a result of myocardial insufficiency. When this is the case expectorants are impotent unless *digitalis* is also used.

Administration.—Expectorants, as a rule, are most effective when administered by the mouth. Sometimes, however, inhala-

tions act beneficially in allaying cough, facilitating expectoration, and lessening fetor of the breath. Except in the case of very volatile substances, it is doubtful whether vapors or sprays penetrate beyond the trachea and the main bronchial divisions. There are several methods of inhalation intended to influence the mucous membrane of the respiratory tract. The simplest plan consists in breathing deeply the warm vapor arising from the surface of boiling water. For this purpose a volatile expectorant—compound tincture of benzoin, terebene, creosote—may be dropped into a wide-mouthed jug nearly filled with hot water, and the vapor conducted to the nose and mouth through a cone made of stiff paper or a folded napkin. Inhalations of this class are rarely useful except in acute bronchitis. More complicated, but somewhat more serviceable, are the various hand-ball and steam atomizers designed to reduce medicated fluids to a nebular form. In chronic bronchitis the cold spray has an advantage over the steam spray in being less relaxing in its effect on the throat and trachea.

Another method of administering medicated vapors is by the so-called respirator. One of the most useful of the latter contrivances is the oronasal respirator devised by Dr. Burney Yeo, which consists of a perforated zinc mask, shaped to fit over the nose and mouth, and held in position by tapes passed around the ears. This mask incloses a sponge which is charged from time to time with the volatile inhalant. Creosote (with an equal amount of spirit of chloroform), oil of turpentine, terebene, eucalyptol, and menthol are the drugs most frequently used in the respirator.

The direct application of drugs to the bronchi by means of intratracheal injections sometimes affords relief in chronic bronchitis and bronchiectasis. If they are skillfully made, they rarely excite cough or other discomfort. A bland oil, such as olive oil, should be made the vehicle for the active drug. The following combination is recommended by T. Grainger Stewart and a number of other writers: Guaiacol, 2 parts; menthol 10 parts; olive oil, 88 parts. About a dram (4 mils) should be injected twice daily.

AMMONII CHLORIDUM, U. S. P.

(Ammonium Chlorid, Sal Ammoniac, NH_4Cl)

Ammonium chlorid is a white, crystalline or granular powder, without odor, of a cooling, saline taste, and permanent in the air. It is soluble in 2.6 parts of water or in 100 parts of alcohol. The dose is from 5 to 15 grains (0.3–1.0 gm.)

PREPARATION

Trochisci Ammonii Chloridi, U. S. P. (each contains ammonium chlorid, $1\frac{1}{2}$ gr.—0.1 gm.; with tragacanth, sugar, and syrup of tolu).

Pharmacologic Action.—When taken by the mouth in moderate doses ammonium chlorid increases and renders less viscid the mucous secretion of the respiratory tract and probably that also of the alimentary canal. Large doses have an irritant action and excite nausea and vomiting. The drug is excreted as ammonium chlorid mainly in the urine, but traces leave the body in the other secretions.

Therapeutics.—Ammonium chlorid is especially useful as an expectorant in the early stages of *acute bronchitis*, when the sputum is scanty and viscid. It is sometimes of service also in *subacute* and *chronic bronchitis* when the secretion is thick and tenacious. In *acute pharyngitis* and *laryngitis* lozenges of ammonium chlorid or a warm spray of the salt (5 gr. to 1 oz.—0.3 gm. to 30.0 mils) may prove beneficial. The drug has found favor with some practitioners in *subacute gastrointestinal catarrh* and in *catarrhal jaundice*.

A solution of ammonium chlorid—5 grain (0.3 gm.) to $\frac{1}{2}$ ounce (15.0 mils) each of alcohol and water—makes a satisfactory lotion in *contusions with ecchymosis*.

Administration.—The drug may be given in aqueous solution, to which licorice is added to disguise its unpleasant salty taste. It may be prescribed also in the form of friable tablets, to be taken after meals in several ounces of water. In many cases of bronchitis ammonium chlorid may be advantageously combined with terpin hydrate or syrup of squill as in the following formulæ:

- ℞. Codeinæ sulphatis..... gr. iii (0.2 gm.)
 Ammonii chloridi
 Terpini hydratis..... āā ʒiiss (6.0 gm.).—M.
 Ponē in capsulas No. xxx.
 Sig.—One capsule every two or three hours.
- ℞. Ammonii chloridi..... ʒiiss (10.0 gm.)
 Tincturæ opii deodorati..... fʒi (4.0 mils)
 Syrupi scillæ..... fʒv (18.5 mils)
 Extracti glycyrrhizæ..... ʒi (4.0 gm.)
 Aquæ..... q. s. ad fʒiv (120.0 mils).—M.
 Sig.—Dessertspoonful in water after meals and at bedtime.

In chronic bronchitis with very tenacious expectoration an iodid may be combined with ammonium chlorid, as in the following formula:

- ℞. Ammonii iodidi..... ʒi (4.0 gm.)
 Ammonii chloridi..... ʒii (8.0 gm.)
 Syrupi pruni virginianæ..... fʒii (60.0 mils)
 Aquæ..... q. s. ad fʒiv (120.0 mils).—M.
 Sig.—A dessertspoonful in water after meals.

Incompatibles.—Alkalis, mineral acids, tartaric acid, and soluble salts of silver and lead.

AMMONII CARBONAS, U. S. P.

(Ammonium Carbonate, NH_4HCO_3 . $\text{NH}_4\text{NH}_2\text{CO}_2$)

The ammonium carbonate of commerce is a mixture of ammonium bicarbonate (acid carbonate) and ammonium carbamate. It occurs in white, translucent masses having a strong ammoniacal odor and a sharp saline taste. It is soluble in about 4 parts of cold water, and is decomposed by boiling water, with the elimination of carbon dioxid and ammonia. On exposure to air it is converted into an opaque white powder of ammonium bicarbonate. The dose is from 5 to 10 grains (0.3–0.6 gm.).

PREPARATION

DOSE

Spiritus Ammoniae Aromaticus, U. S. P. (ammonium carbonate, 3.4; ammonia water, 9; aromatic oils; water to make 100 parts) 20–60 min. (1.3–4.0 mls).

Pharmacologic Action.—In therapeutic doses ammonium carbonate acts as a circulatory stimulant, a respiratory stimulant, and an expectorant. Its effects on the circulation and respiration are mainly reflex and the result of its local irritant action. They appear quickly, but are extremely evanescent. The drug owes its expectorant properties partly to its irritant or nauseating effects, and partly, perhaps, to the action of ammonium chlorid, into which a small proportion is transformed by the hydrochloric acid of the stomach. Large doses of ammonium carbonate are irritant and produce emesis. The drug is excreted in the urine chiefly as urea.

Therapeutics.—Ammonium carbonate may be substituted for the water or the aromatic spirit of ammonia in combating *syncope* and *other forms of sudden heart failure*. It is often prescribed as an expectorant in *bronchitis*, *bronchopneumonia*, and even *lobar pneumonia*, when there is much bronchial catarrh, but it is less reliable than ammonium chlorid and more irritant to the stomach. In *pulmonary emphysema*, when there is marked dyspnea and cyanosis, as a result of an exacerbation of the associated bronchial catarrh, it acts very well in conjunction with digitalis and strychnin.

Mixed with half its bulk of stronger water of ammonia and scented with oil of lavender, it constitutes the “smelling-salts,” a popular remedy for *fainting*.

Administration.—Ammonium carbonate should be prescribed in solution, and because of its ephemeral action it should be given at comparatively short intervals.

Incompatibles.—It is incompatible with acids, acid salts, alkaloidal salts, and most metallic salts. It is decomposed by syrup of squill, as the latter being made of the vinegar squill, contains free acetic acid.

ANTIMONII ET POTASSII TARTRAS, U. S. P.

(Tartar Emetic, $2K(SbO)C_4H_4O_6 + H_2O$)

Tartar emetic is the only official preparation of antimony. It occurs in the form of colorless crystals or a white granular powder, having a sweetish metallic taste, soluble in 12 parts of cold water and insoluble in alcohol. The dose as an expectorant is $\frac{1}{20}$ to $\frac{1}{8}$ grain (0.003–0.008 gm.); as an emetic, $\frac{1}{2}$ to 1 grain (0.03–0.06 gm.).

PREPARATIONS

DOSE

Syrupus Scillæ Compositus, U. S. P. (0.2 per cent. with squill and senega).....	10–60 min. (0.6–4.0 mls)
Vinum Antimonii, U. S. P. (0.4 per cent.).....	10–20 min. (0.6–1.2 mls)

Tartar Emetic (0.024 per cent.) is also contained in compound licorice mixture.

Pharmacologic Action.—Save that it is more irritant and is absorbed with greater difficulty, tartar emetic, like other antimonial preparations, has an action similar to that of arsenic. When applied to the skin in ointment it produces papules, vesicles, pustules, and, if the contact be prolonged, diffuse abscesses. Taken internally in small doses ($\frac{1}{8}$ – $\frac{1}{4}$ gr.—0.008–0.016 gm.) it causes nausea and some increase in the perspiration and secretions of the mouth and respiratory tract. Large doses (1–2 gr.—0.065–0.13 gm.) produce persistent vomiting with salivation, copious sweating, and marked depression. Still larger doses are followed by choleraic discharges from the bowel, painful cramps, and collapse.

The emesis occasioned by tartar emetic is probably the result of the direct irritant action of the drug on the stomach, though some writers believe that it is partly of cerebral origin. The marked depression and ultimate collapse after large doses are due partly to the violent emesis, partly to paralysis of the vessels of the splanchnic area, and partly to weakening of the heart itself. In fatal poisoning postmortem examination reveals intense congestion of the alimentary canal with hemorrhagic extravasations, and also cloudy swelling and fatty degeneration of the parenchymatous organs. Antimony is excreted chiefly by the stomach and bowel, but in small part by the kidneys, skin, and respiratory tract.

The *treatment of antimonial poisoning* consists in the administration of tannin to form an insoluble salt, in washing out the stomach, and in combating collapse with diffusible stimulants and external heat.

Therapeutics.—Tartar emetic is an efficient expectorant in *acute bronchitis* when there is harassing cough with little or no expectoration. It may be prescribed conveniently in the form of wine of antimony, as in the following formula:

R. Vini antimonii..... f℥ij (8.0 mls)
 Spiritus ætheris nitrosi..... f℥j (30.0 mls)
 Tincturæ opii camphoratæ..... f℥ss (15.0 mls)
 Liquoris potassii citratis... q. s. ad f℥iv (120.0 mls).—M.
 Sig.—A dessertspoonful in water every two or three hours.

Somewhat favorable reports have recently been made upon the use of tartar emetic in *kala-azar*, *trypanosomiasis* and *schistosomiasis (bilharziasis)*. The drug is given intravenously in doses of $\frac{1}{2}$ grain (0.03 gm.), increased to 2 grains (0.13 gm.), in 5 ounces (150.0 mls) of saline solution, care being taken not to allow any of the fluid to enter the subcutaneous tissues, as it is likely to cause necrosis. The injections are given every day or every other day until 20 or 25 grains (1.3–1.6 gm.) in all have been taken.

Tartar emetic was formerly used also as an emetic, a diaphoretic, a circulatory depressant and a counterirritant, but for these purposes it has been displaced by more effective and less poisonous remedies.

Incompatibles.—Tartar emetic is incompatible with tannin, mineral acids, alkaline carbonates and lime-water.

IPPECACUANHA, U. S. P.

(Ipecac)

Ipecac is the root of *Cephaelis Ipecacuanha* or of *Cephaelis acuminata*, perennial shrubs growing in Brazil and other South American states. It contains several alkaloids, of which two, *emetin* and *cephaelin*, have an emetic action. The dose of powdered ipecacuanha as an emetic is from 15 to 30 grains (1.0–2.0 gm.); as an expectorant, $\frac{1}{2}$ to 2 grains (0.032–0.13 gm.).

Emetin is official as the hydrochlorid (*Emetinæ Hydrochloridum*, U. S. P.), which occurs as a white crystalline powder, freely soluble in alcohol or water. The average dose is $\frac{1}{3}$ grain (0.02 gm.).

PREPARATIONS

DOSE

Fluidextractum Ipecacuanhæ, U. S. P.....	1-2 min. (0.06-0.12 mil)
Syrupus Ipecacuanhæ, U. S. P.....	As an expectorant, 10-60 min. (0.6-4.0 mils); as an emetic, 2-4 fl. dr. (8.0- 15.0 mils)
Pulvis Ipecacuanhæ et Opii, U. S. P. (Dover's powder: ipecac, 1 part; powdered opium, 1 part; sugar of milk, 8 parts).....	5-10 gr. (0.3-0.6 gm.).

Pharmacologic Action.—Ipecac is a powerful local irritant. When rubbed into the skin it causes erythema and vesication; when applied to mucous membranes it produces redness, swelling, and an increase of secretions. In some persons the mucous membrane of the respiratory tract is so sensitive to the drug that the inhalation of an exceedingly small quantity of the powder is sufficient to excite lachrymation, sneezing, running from the nose, and even asthmatic breathing. The ingestion of a full dose of ipecac is followed in about half an hour by nausea, vomiting, and an increase of the secretions of the nose, mouth and bronchi. These effects are due to emetin and cephaelin, which have a similar action, although the latter is much more powerful than the former. The emesis is due chiefly to the local irritant action of the drug, but as vomiting movements occur even after removal of the stomach, it must be partly of central origin. Emetin has considerable bactericidal power, and even in comparatively weak solutions it is destructive to *entamoeba histolytica* and other amebæ. The amebacidal power of cephaelin is much less than that of emetin.

Administered subcutaneously in toxic doses, emetin causes hemorrhagic gastro-enteritis, muscular paralysis, renal insufficiency, stupor, and collapse.

Therapeutics.—Ipecac is chiefly employed as a sedative expectorant, an emetic, an antiemetic, an amebacide, and a diaphoretic.

Expectorants.—Ipecac is one of the most reliable of the expectorants in *acute bronchitis* before secretion is well established.

Emetic.—Ipecac, although not very prompt in its action, is a certain and safe emetic. It is especially useful, in children, in whom it is frequently employed to unload the stomach of irritant material. In poisoning more quickly acting emetics, such as apomorphin or zinc sulphate, are preferable.

Anti-emetic.—Ipecac in minute doses is sometimes of service in controlling *persistent vomiting* occurring in diseases of the stomach not associated with active inflammation. There is no adequate explanation of its antiemetic action. The drug may be given as ipecac, in doses of $\frac{1}{8}$ to $\frac{1}{4}$ grain (0.008-0.016 gm.)

or as the wine of ipecac, in doses of 1 minim (0.06 mil) every half hour.

Amebacide.—Ipecac has been used empirically in the treatment of dysentery since the seventeenth century, but it is only in the *amebic variety* that it has given good results. Its efficacy is due to the specific amebacidal properties of emetin. Formerly, ipecac itself was used, from 30 to 45 grains (2.0–3.0 gm.) being given at night, three hours after the last meal, and this dose being gradually reduced to 20 grains (1.3 gm.) over a period of about a week. The minimal dose was then given for another week. To prevent vomiting the drug was given in salol-coated pills or was preceded by tincture of deodorized opium (20 min.—1.3 mils).

In 1912 Rogers recommended the use of emetin hydrochlorid hypodermically, and this method of treatment soon supplanted the use of ipecac by the mouth, as it proved to be less unpleasant and more effective. The usual dosage is $\frac{1}{2}$ grain (0.03 gm.) twice daily, or 1 grain (0.065 gm.) once a day, for ten days or two weeks. If colic or severe diarrhea supervenes it may be checked by opium and bismuth subcarbonate. After the symptoms have entirely subsided, a stool obtained by the use of a saline cathartic should be examined once a month for several months, and if amebæ are found the treatment should be repeated. Some observers have found that relapse, which is not uncommon, is less likely to occur if ipecac, 30 to 60 grains (2.0–4.0 gm.), in salol-coated pills, is given for a few days after the discontinuance of the emetin. Both emetin and ipecac often prove ineffectual in both extremely acute and extremely chronic cases of amebiasis, as well as in carriers.

The effects of emetin must always be carefully observed, as the preparations seem to vary in strength, and poisoning has been somewhat frequent. The most common toxic effects are diarrhea, abdominal pain, albuminuria, muscular weakness, and neuritic pains. A case of fatal poisoning has been reported by Levy and Rowntree.

Emetin has given good results also in the *presuppurative stage of amebic hepatitis*. Even after the occurrence of an actual abscess in the liver, it may be employed as an adjuvant to surgical treatment. The drug has been advocated in the treatment of *pyorrhea alveolaris*, because amebæ have been found in the lesions of this disease. The evidence that the amebæ are the cause of the pyorrhea is, however, far from conclusive.

Diaphoretic.—The mild and agreeable diaphoretic effect of ipecac in the form of Dover's powder has made the latter a favorite remedy in the initial stage of *acute coryza*, in *myalgia from chilling*, in *influenza*, and in *acute suppression of the menses*.

Other Uses.—Ipecac has been employed in *hemoptysis* and other internal hemorrhages since Trousseau's time, but its use as a hemostatic rests upon no rational basis, and is of doubtful value. In minute doses ($\frac{1}{8}$ – $\frac{1}{4}$ gr.—0.008–0.016 gm.), it has been recommended as an adjuvant to strychnin in *indigestion dependent upon motor insufficiency*. In *atony of the bowel* it often makes a useful addition to cathartic pills.

Administration.—For producing emesis either ipecac itself or the syrup may be selected; in children the syrup, $\frac{1}{2}$ to 2 fluidrams (2.0–8.0 mls), is preferable. Paul and Cownley recommend cephaelin as a powerful and certain emetic, free from depressing effects when given in doses of from $\frac{1}{10}$ to $\frac{1}{5}$ grain (0.006–0.01 gm.), but it is too costly for ordinary use. As an expectorant the wine, syrup, or fluid extract may be employed. A combination of ipecac with an alkaline expectorant, as in the following formula, is often effective in the first stage of bronchitis:

R̄. Potassii citratis ʒiii (12.0 gm.)
 Tincturæ opii camphoratæ..... f ʒv (18.5 mls)
 Syrupi ipecacuanhæ..... f ʒvi (22.5 mls)
 Aquæ..... q. s. ad f ʒvi (180.0 mls).—M.
 Sig.—A tablespoonful every three or four hours.

Emetin Bismuth Iodid.—This preparation is only slightly soluble in the acid juice of the stomach, but it is readily soluble in the alkaline juice of the intestine. For this reason it was supposed that the drug would be free from the nauseant and emetic actions of emetin and ipecac. Experience has shown, however, that while it is an energetic amebacide, it is by no means devoid of irritant properties and that it often causes both vomiting and diarrhea. It seems to be as efficacious in *acute amebic dysentery* as emetin given hypodermically, and more efficacious than that drug in removing the cysts from the feces of *chronic carriers*. The usual dosage of emetin bismuth iodid is from 2 to 4 grains (0.13–0.26 gm.), in capsules, once daily, after the mid-day meal, for twelve successive days. Three grains (0.2 gm.) of the drug correspond to about 1 grain (0.065 gm.) of emetin.

SCILLA, U. S. P.

Squill is the bulb of *Urginea maritima*, a perennial herb growing on the shores of the Mediterranean Sea. Its active principles are glucosids, but it is doubtful whether these have been isolated in pure form. The dose of powdered squill is from 1 to 3 grains (0.065–0.2 gm.).

PREPARATIONS	DOSE
Acetum Scillæ, U. S. P.	10-30 min. (0.6-2.0 mils)
Fluidextractum Scillæ, U. S. P.	1-3 min. (0.06-0.2 mil)
Tinctura Scillæ, U. S. P.	5-20 min. (0.3-1.2 mils)
Syrupus Scillæ, U. S. P. (from the vinegar)....	$\frac{1}{2}$ -1 fl. dr. (2.0-4.0 mils)
Syrupus Scillæ Compositus, U. S. P. (fluidext. of squill 8 per cent.; fluidext. of senega 8 per cent.; tartar emetic 0.2 per cent.).....	10-60 min. (0.6-4.0 mils).

Pharmacologic Action and Therapeutics.—Squill has an action on the circulation similar to that of digitalis, but is more irritant to the gastrointestinal tract and less certain of absorption. Like digitalis, it produces diuresis only indirectly by improving the circulation and relieving general venous congestion. Large doses of the drug cause vomiting and purging.

Squill is employed chiefly as an expectorant and diuretic. As an expectorant, it is useful in the form of the syrup or compound syrup in *bronchitis* with scanty and tenacious sputum. It is some times very effective in persistent bronchitis accompanying myocardial disease. The simple syrup, being made of the vinegar of squill, is incompatible with ammonium carbonate. It may be prescribed, however, with ammonium chlorid.

As a diuretic, squill is sometimes of service in *dropsy of cardiac origin*. It is usually prescribed in the form of Niemeyer's or Guy's pill (see p. 46), or a modification of it, such as the following:

℞. Pulveris scillæ
Pulveris digitalis
Hydrargyri chloridi mitis
Caffeinæ citratæ..... ̄ā gr. xii (0.8 gm.).—M.
Pone in capsulas No. xii.
Sig.—One capsule three times a day.

ASPIDOSPERMA, U. S. P.

(Quebracho)

Aspidosperma is the dried bark of *Aspidosperma Quebracho blanco*, an evergreen tree growing in South America. It contains several alkaloids, the most important of which is *aspidospermin*. The aspidospermin of commerce, however, is really a mixture of the various alkaloids and may be given in doses of $\frac{1}{2}$ to 1 grain (0.03-0.065 gm.).

PREPARATION	DOSE
Fluidextractum Aspidospermatis, U. S. P.	$\frac{1}{2}$ -1 fl. dr. (2.0-4.0 mils).

Pharmacologic Action and Therapeutics.—In large doses the alkaloids of aspidosperma have an action similar to that of nicotin, that is, they depress the autonomic ganglia, both sympathetic and parasympathetic, and first stimulate and then depress

the entire central nervous system. One alkaloid, aspidosamin, is an active emetic. In therapeutic doses aspidospermin is a respiratory stimulant. Aspidosperma has been employed with some success as an expectorant and respiratory stimulant in *bronchitis associated with asthma or emphysema*.

SANGUINARIA, U. S. P.

(Bloodroot)

Sanguinaria is the dried rhizome and roots of *Sanguinaria canadensis*, a perennial herb growing in the woods of North America. It contains an alkaloid, *sanguinarin*.

PREPARATION

DOSE

Tinctura Sanguinariae. 10–30 min. (0.6–2.0 mls).

Pharmacologic and Therapeutics.—Sanguinaria has an irritant action, and in large dose excites nausea and vomiting. The alkaloid sanguinarin has an action similar to that of some of the minor opium alkaloids. It depresses slightly the cerebrum and at the same time stimulates the spinal cord, causing in toxic doses tetanic convulsions. It also depresses the heart. It has been employed both as an emetic and expectorant, but it has been supplanted by more efficient remedies.

EUCALYPTUS, U. S. P.

(Blue Gum Leaves)

Eucalyptus is the leaves of *Eucalyptus Globulus*, or gum-tree, a native of Australia and largely cultivated in Europe and Southern United States. It contains a volatile oil (6 per cent.), from which is obtained a stearopten, *eucalyptol*. The latter is a colorless liquid having a camphoraceous odor and a pungent spicy taste, and on exposure to a temperature below 30° F. solidifying into a mass of needle-shaped crystals. It is insoluble in water, but soluble in alcohol. The dose of either the oil of eucalyptus or of eucalyptol is from 3 to 10 minims (0.2–0.6 mil).

PREPARATION

DOSE

Fluidextractum Eucalypti, U. S. P. . . . 20–60 min. (1.2–4.0 mls).

Pharmacologic Action.—Oil of eucalyptus is a local irritant. When applied to the skin, evaporation being prevented, it causes redness and sometimes vesication. When taken internally in large doses (20 min.—1.2 mls) it causes a sense of burning in the throat and stomach, nausea, looseness of the bowels, and slight mental exhilaration, which in turn is followed by a sense of calm. Toxic doses cause vomiting, diarrhea, coma and collapse. Occa-

sionally, dermatitis is also seen. The drug is eliminated in all the secretions, and, like oil of turpentine, imparts an odor of violets to the urine.

Both eucalyptol and the oil have pronounced antiseptic properties.

Therapeutics.—Oil of eucalyptus is a useful expectorant in *subacute* and *chronic bronchitis* attended with copious mucopurulent expectoration. As an inhalant, eucalyptol is sometimes of service in decreasing the profuse expectoration in *bronchiectasis* and *pulmonary tuberculosis*. Half a dram (2.0 mils) may be added to an ounce (30.0 mils) of liquid petrolatum and used in an atomizer; or oil of eucalyptus alone, or in conjunction with terebene, may be used in an oro-nasal respirator.

Eucalyptol in the form of an oil spray often acts favorably in *subacute* and *chronic rhinitis*, if used after the nares have been thoroughly cleansed with an alkaline wash. The following formula, suggested by Douglass, illustrates this use:

R.	Thymolis.....	gr. x (0.65 gm.)
	Mentholis.....	gr. xx (1.3 gm.)
	Eucalyptolis.....	gtt. xx (0.6 mil)
	Olei cubebæ.....	gtt. xl (1.2 mils)
	Benzoinol.....	f 3 vj (175.0 mils).—M.

Oil of eucalyptus is sometimes used as a urinary antiseptic in *cystitis* and *urethritis*. Eucalyptol has been employed as a solvent for dichloramin-T.

Administration.—The oil and eucalyptol are the best-preparations for internal use. They may be given on sugar, in capsules, or in an emulsion.

OLEUM MYRTI

(Oil of Myrtle, Myrtol)

Oil of myrtle is a greenish-yellow, volatile oil, distilled from the leaves and flowers of *Myrtus communis*, the common European myrtle. It has properties almost identical with those of eucalyptol. The dose is from 3 to 10 minims (0.2–0.6 mils). It is a reliable stimulant expectorant in *bronchorrhea* and *bronchiectasis*. Eichhorst has used it with satisfaction in *pulmonary gangrene*.

BENZOINUM, U. S. P.

(Benzoin, Gum Benzoin)

Benzoin is a balsamic resin obtained from *Styrax Benzoin*, a large tree growing in Sumatra, Java, Borneo, and Siam. It contains several resins, benzoic acid (15–20 per cent.), a vola-

tile oil, cinnamic acid, and vanillin. It is soluble in about 5 parts of warm alcohol and in solutions of the fixed alkalis. Benzoic acid is soluble in 2.3 parts of alcohol and very sparingly soluble in water. The salts of benzoic acid—ammonium, lithium, and sodium—are readily soluble in water.

PREPARATIONS	DOSE
Tinctura Benzoini, U. S. P.....	20–60 min. (1.2–4.0 mils)
Tinctura Benzoini Composita, U. S. P. (Friar's or Turlington's Balsam: 10 per cent., with aloes, tolu, and storax).....	20–60 min. (1.2–4.0 mils)
Adeps Benzoinatus, U. S. P. (2 per cent.)	
Acidum Benzoicum, U. S. P.....	5–20 gr. (0.3–1.3 gm.)
Ammonii Benzoas, U. S. P.....	5–30 gr. (0.3–2.0 gm.)
Sodii Benzoas, U. S. P.....	5–30 gr. (0.3–2.0 gm.)
Lithii Benzoas.....	5–30 gr. (0.3–2.0 gm.).

Benzoic acid (0.4 per cent.) also enters into camphorated tincture of opium, or paregoric.

Pharmacologic Action.—Benzoic acid is an antiseptic of considerable power and a stimulant to the mucous membranes. In health moderate doses do not affect the functions of the body beyond increasing, to a variable degree, the nitrogenous output and lessening the quantity of ethereal sulphates and of indican in the urine. It escapes from the body rapidly, chiefly through the kidneys, and for the most part in the form of hippuric acid—a compound of benzoic acid with the protein derivative, glycocholl. Large doses of the drug produce symptoms similar to those of salicylism and sometimes excite nausea and vomiting. Used as food preservatives in amounts not exceeding 8 grains (0.5 gm.) a day, the benzoates are apparently innocuous.

Therapeutics.—The compound tincture of benzoin painted over the part and allowed to dry is a useful *protective for small wounds*. A combination of the compound tincture with 4 parts of glycerin makes an efficient application in *chapped nipples, hands, or lips*. A dram (4.0 mils) to a pint (0.5 L.) of boiling water may be used as an inhalant in *acute laryngitis* and *bronchitis*. The tincture may be prescribed internally also in *subacute* and *chronic bronchitis* when expectoration is very viscid. Benzoic acid itself sometimes affords relief in *phosphaturia*, and in *cystitis with ammoniacal urine*. Sodium benzoate, in doses of from 5 to 10 grains (0.3–0.6 gm.), is a useful remedy in *acute pharyngitis* and *tonsillitis*.

Owing to the fact that benzoic acid is eliminated as the soluble hippuric acid, it was hoped that the benzoates would prove of value in gout, but experience has shown that they are of no avail. Senator and others have recommended the benzoates

in rheumatism, but they have been found to be much less efficacious than the salicylates.

Administration.—Benzoic acid is best administered in capsules or pills. The benzoates may be administered in solution or in powders. The tinctures are incompatible with aqueous preparations.

BALSAMUM PERUVIANUM, U. S. P.

(Balsam of Peru)

Balsam of Peru is a brownish-black, syrupy liquid, obtained by bruising the bark of *Toluiфера Pereira*, a large tree growing in Central America. It has a smoky, vanilla-like odor and a bitter, persistent taste. It is soluble in alcohol, chloroform, or glacial acetic acid. It contains resins, cinnamic and benzoic acids, and traces of vanillin. The dose is from 5 to 30 minims (0.3–2.0 mls).

Therapeutics.—Balsam of Peru is chiefly employed externally as a protective and parasiticide. It was at one time used as a stimulant expectorant in *chronic bronchitis*, but it has been entirely replaced by more efficient remedies. It is still occasionally employed as a stimulant protective dressing in *bed-sores* and *other ulcers*. Alone, or in combination with sulphur, it is a reliable remedy in *scabies*, in which disease it may be prescribed as follows:

℞. Sulphuris præcipitati
Balsami peruviani.....āā 3ij (8.0 gm.)
Olei olivæ.....f℥ss (15.0 mls)
Adipis.....q. s. ad 3ij (60.0 gm.).—M.

BALSAMUM TOLUTANUM, U. S. P.

(Balsam of Tolu)

Balsam of Tolu is a yellowish-brown, semiliquid mass, obtained by incising the bark of *Toluiфера Balsamum*, an ever-green tree growing in South America. It has a vanilla-like odor and a mild, aromatic taste, and is soluble in alcohol, ether, or chloroform, but is insoluble in water. It contains resin, a volatile oil, vanillin, and cinnamic and benzoic acids. The dose is from 5 to 30 grains (0.3–2.0 gm.).

PREPARATIONS	DOSE
Syrupus Tolutanus, U. S. P.....	1–4 fl. dr. (4.0–15.0 mls)
Tinctura Tolutana, U. S. P.....	½–1 fl. dr. (2.0–4.0 mls)
Tinctura Benzoini Composita, U. S. P. (4 per cent.).....	20–60 min. (1.2–4.0 mls).

Therapeutics.—Balsam of tolu has but feeble medicinal properties. The syrup is often employed on account of its agreeable flavor in cough-mixtures.

PIX LIQUIDA, U. S. P.

(Tar)

Tar is an empyreumatic oleoresin obtained by the destructive distillation of *Pinus palustris* and of other species of *Pinus*. It is a thick, blackish-brown liquid, having a terebinthinate odor and a pungent taste. It is only slightly soluble in water, but it is freely miscible with oils, alcohol, ether or chloroform. Its active constituents are guaiacol and creosols. When subjected to distillation it yields a volatile oil—*oil of tar*. The dose is from 3 to 15 grains (0.2–1.0 gm.).

PREPARATIONS

DOSE

Oleum Picis Liquidæ Rectificatum, U. S. P.....	1–5 min. (0.06–0.3 mil)
Syrupus Picis Liquidæ, U. S. P.....	1–2 fl. dr. (4.0–8.0 mls).
Unguentum Picis Liquidæ, U. S. P. (50 per cent.).	

A water (Aqua Picis Liquidæ) is also in use. It is made by shaking together 1 part of tar and 4 parts of water frequently for twenty-four hours, decanting and filtering. The dose is from 1 to 4 fluidounces (30.0–120.0 mls).

Pharmacologic Action and Therapeutics.—Tar is a local stimulant and an antiseptic. It is chiefly employed in medicine as an expectorant and as a local remedy in certain chronic inflammatory skin diseases. It is an indifferent expectorant, although it sometimes succeeds in *chronic bronchitis with abundant sputum* and *harassing cough* after other remedies have failed. It may be given in pills or capsules, or in the form of the syrup or the water of tar. Murrell has found inhalations of tar water also useful in the same class of cases.

In *chronic eczema* and *psoriasis*, when the lesions are sluggish, an ointment of tar makes a useful application; the official ointment is usually too strong, $\frac{1}{2}$ to 2 drams (2.0–8.0 gm.) to the ounce (30.0 gm.) of lard being quite sufficient in the majority of cases. It should always be used tentatively, as in some persons the skin is exceedingly sensitive to the drug. It is absolutely contraindicated if the inflammatory process is at all active.

GRINDELIA, U. S. P.

Grindelia is the leaves and flowering tops of *Grindelia camporum* and *Grindelia squarrosa*, perennial herbs growing in North America, west of the Rocky Mountains. It contains resin, a bitter principle, and a volatile oil of a terebinthinate odor.

PREPARATION

DOSE

Fluidextractum Grindeliæ, U. S. P.... 15-60 min. (1.0-4.0 mils).

Therapeutics.—Grindelia is a useful remedy in *bronchitis complicated with asthma*. It may be prescribed alone or in combination with other antiasthmatics, as in the following formula:

℞. Sodii iodidi..... ʒj (4.0 gm.)
 Fluidextracti grindeliæ..... f ʒss (15.0 mils)
 Tincturæ lobeliæ
 Tincturæ belladonnæ..... āā f ʒij (8.0 mils)
 Syrupi tolutani..... q. s. ad f ʒiij (90.0 mils).—M.
 Sig.—A teaspoonful every three or four hours.

The fumes of burning grindelia leaves are also efficacious in allaying the cough and relieving the dyspnea of asthma. A lotion consisting of an ounce (30.0 mils) of the fluid extract to a pint of water (0.5 L.) has been highly recommended in *rhus poisoning* and *erysipelas*. It should be applied on cloths and allowed to evaporate.

OTHER EXPECTORANTS

Apomorphin Hydrochlorid (see p. 184).—This artificial alkaloid is chiefly interesting as a centrally acting emetic. Administered by the mouth, in doses of $\frac{1}{30}$ to $\frac{1}{10}$ grain (0.002-0.006 gm.), it has been employed to some extent as a sedative expectorant in *acute bronchitis*, but it is less effective than many of the other nauseants.

Apocodein Hydrochlorid.—This artificial alkaloid is prepared from codein after the manner of preparing apomorphin from morphin. It is an amorphous powder, soluble in water or alcohol. It has an action similar to that of apomorphin and is said also to be depressant to sympathetic nerve-endings.

Lobelia (see p. 157).—Lobelia, like other nauseants, increases the bronchial secretion. In large dose it also depresses the fibers of the vagus distributed to the bronchial muscles. Owing to this combined action, the drug is especially valuable in *bronchitis with asthma*. The dose of the tincture of lobelia as an expectorant is from 10 to 30 minims (0.6-2.0 mils); of the fluid-extract, from 2 to 5 minims (0.1-0.3 mils).

Potassium Citrate (see p. 247).—This and other organic salts of potassium are very useful expectorants in the early stages of *acute bronchitis*. The citrate is generally preferred to the other salts, owing to its less unpleasant taste. It may be prescribed in doses of from 20 to 30 grains (1.3-2.0 gm.), in combination with a nauseant such as ipecac or antimony.

Oil of Santal (see p. 254).—When pure, this drug often proves to be a useful expectorant in *subacute* and *chronic bronchitis* with profuse purulent sputum. Its chief drawback is its tendency to disturb the stomach. It should be given in doses of from 5 to 15 minims (0.3–1.0 mil) in capsules or in emulsion. Terebene and oil of eucalyptus are efficient synergists.

Copaiba and Cubeb (see pp. 252 and 253).—The oil of copaiba and oleoresin of cubeb have been employed as expectorants in *chronic bronchitis with profuse purulent sputum*, but they are neither so efficacious nor so agreeable as terebene, oil of eucalyptus, and the preparations of guaiacol. Smoking cigarettes containing cubeb sometimes affords relief in the paroxysms of *asthma*. Lozenges of cubeb are useful in relieving hoarseness and fatigue of the larynx resulting from prolonged use of the voice.

Oil of Turpentine (see p. 254).—This drug, once much used as an expectorant in *chronic bronchitis*, has been largely replaced by terebene and terpin hydrate. Terebene (*Terebenum*, U. S. P.) is a liquid hydrocarbon made by oxidizing oil of turpentine with strong sulphuric acid. The dose is from 5 to 10 minims (0.3–0.6 mil). Terpin hydrate (*Terpini Hydras*, U. S. P.) is a crystalline compound obtained by the interaction of oil of turpentine, alcohol and nitric acid. The dose is from 2 to 10 grains (0.13–0.6 gm.). Terebene is one of the most satisfactory remedies that we possess in *bronchitis* with free expectoration. In *pulmonary tuberculosis*, also, it is often of service when the catarrhal symptoms are prominent. In moderate doses it is usually well borne but large doses may excite nausea or irritation of the kidneys and bladder. As it is insoluble in water, it should be given in capsules, on sugar, in an emulsion, or in an elixir. It may also be inhaled, either as a fine spray or from the sponge of an oronasal respirator.

Terpin hydrate has therapeutic properties similar to those of terebene, but it is less active. It may be given in pills, in capsules, or in an elixir.

Creosote (see p. 408).—This drug and its derivatives are useful expectorants in *chronic bronchitis* and *bronchiectasis with copious purulent sputum*. So long ago as Addison's time creosote was used as a remedy for *pulmonary tuberculosis*. This use was revived by Bouchard and Gembert in 1877, and again by Sommerbrodt in 1887. While it has been shown conclusively that the drug has no specific influence, the testimony of numerous clinicians is convincing that it is often effective in the later stages of the disease in allaying cough and decreasing the sputum, when this is abundant and purulent. There is rarely any

indication for its use in the early stages of the disease. Inhalations of creosote are frequently efficacious in *laryngitis*, *bronchitis*, *bronchiectasis*, and *pulmonary tuberculosis*. Ten minims (0.6 mil) of creosote to 10 ounces of boiling water (300.0 mls) makes a suitable mixture for inhalation when the catarrhal process is acute. A mixture of equal parts of creosote and spirit of chloroform, employed in a respirator, sometimes serves to control painful paroxysms of cough in tuberculosis.

Guaiacolis Carbonas, U. S. P.—Carbonate of guaiacol is produced by the action of carbonyl chlorid on the sodium salt of guaiacol. It is a white crystalline powder, odorless and almost tasteless. It is insoluble in water, and is but slightly soluble in alcohol. The dose is from 5 to 20 grains (0.3–1.3 gm.), thrice daily. As carbonate of guaiacol passes through the stomach unchanged and is decomposed into its constituents very slowly in the intestine, it is comparatively free from irritant or toxic properties. Not rarely after large doses a certain amount escapes in the feces undecomposed. Guaiacol carbonate is an excellent expectorant in *bronchitis*, *bronchiectasis* and *pulmonary tuberculosis* with copious mucopurulent sputum. On account of its freedom from odor, taste and irritant properties it is much better borne than creosote. In doses of 10 grains (0.65 gm.), gradually increased to 20 grains (1.3 gm.), thrice daily, it has been highly recommended by Luff and others in *rheumatoid arthritis*. As it undergoes decomposition slowly in the intestine, it may be employed also as an *intestinal antiseptic*. It may be prescribed in pills, capsules or powders. In catarrhal conditions of the respiratory tract it may be combined with other stimulant expectorants, as in the following formula:

℞. Codeinæ sulphatis..... gr. ii (0.13 gm.)
 Terebeni..... f ʒiiss (6.0 mls)
 Guaiacolis carbonatis..... ʒiiss (10.0 gm.).—M.
 Ponē in capsulas No. xl.
 Sig.—Two capsules after each meal and at bedtime.

Creosoti Carbonas, U. S. P.—Creosote carbonate (creosotal) is an oily liquid containing a mixture of the carbonates of the various phenols, chiefly, guaiacol and creosol, present in creosote. It is an oily liquid, odorless, and almost tasteless. It is insoluble in water and freely soluble in alcohol. It has advantages over creosote in having but little taste and in being more acceptable to the stomach. The dose is from 3 to 5 minims (0.2–0.3 mil), gradually increased to 20 minims (1.3 mls). It may be given in capsules, or in milk or claret.

Carbonate of creosote may be employed in the same class of cases as creosote and guaiacol carbonate.

TONICS

Tonics are drugs that impart strength or tone to the system. In one sense every drug that favorably influences disease is a tonic, since, by removing the cause of debility, it serves to restore normal vitality. The term, however, is customarily restricted to remedies that have a more or less general invigorating effect, without necessarily exerting a specific influence on any one organ. A more exact knowledge of the pharmacologic action of drugs and a clearer appreciation of the primary causes of general weakness and malnutrition have tended to diminish gradually, but steadily, the number of remedies grouped under this heading. The following drugs may still be classed conveniently as tonics:

Iron.
Phosphorus.
Cod-liver oil.

Nux vomica, *cinchona*, and *arsenic* also exert a tonic influence, but as this is subordinate to their other actions, these drugs have been considered in other groups.

FERRUM, U. S. P.

(Iron, Fe)

Iron is official in the form of fine, bright, non-elastic wire.

Pharmacologic Action.—As iron is a constituent of the normal body, it may be regarded as a food as well as a medicine. It is especially abundant (0.4 per cent.) in hemoglobin, and its presence in this compound is intimately associated with the function of the red corpuscles to carry oxygen from the lungs to the tissues. When iron is taken in therapeutic doses it acts as an astringent, causing more or less constipation. Large doses have an irritant effect and disturb digestion. It is now definitely known that both inorganic and organic preparations of the metal are capable of absorption. Only a small portion, however, of the quantity ingested enters the blood, the larger portion being discharged from the bowel unchanged or as a sulphid, the stools, owing to the presence of the latter, acquiring a blackish color. Absorption takes place mainly in the duodenum, the iron entering the general circulation probably as an albuminate. According to Macallum, transportation is effected through the agency of the leukocytes, and, more especially, of the blood-plasma. The amount that is absorbed varies somewhat with the nature of the preparation and the quantity that is administered. From the blood the iron is deposited in organic form in the liver, bone-

marrow, mesenteric lymph-nodes, and kidneys, and especially in the spleen, where it remains as a "reserve," which is drawn upon from time to time to supply the needs of the organism. The reserve rapidly disappears in acute posthemorrhagic anemia during regeneration of the blood. The synthesis of the iron to hemoglobin takes place in the red bone-marrow, although it is likely that other organs take part in the formation of intermediate products. Excretion occurs mainly by the intestinal epithelium, only minute quantities of the metal leaving the body by the urine. Even when the drug is injected directly into a vein it is excreted almost entirely in the feces.

In health the iron naturally contained in food is all-sufficient for the needs of the system, and the administration of medicinal iron is not followed by any notable increase in the number of red blood-cells or their hemoglobin value. In certain forms of anemia, however, especially chlorosis, chalybeate preparations increase the amount of hemoglobin and, to a less extent, the number of red blood-cells. Whether the drug acts simply by furnishing material for the corpuscles or by stimulating the functional activity of the blood-making organs is not definitely known. Administered intravenously in large doses, iron is distinctly poisonous, producing effects similar to those of arsenic.

Untoward Effects.—The continued use of iron, especially of the ferric salts, frequently excites indigestion, constipation and headache. Iron salts of the mineral acids also have a decided tendency to corrode the enamel of the teeth.

Therapeutics.—The most important indication for the use of iron is *anemia*. The best effects are seen in *chlorosis*, in which disease the drug has almost a specific action. In *secondary anemia* the results of its use are less decisive, but after the removal of the cause it serves to hasten the restoration of the blood to its normal condition. Iron plays indirectly the part of an emmenagogue in *amenorrhea* dependent upon anemia. The ferrous and ferric salts of the mineral acids are used as *astringents* and *styptics*, and the freshly precipitated ferric hydroxid is used as an antidote in *arsenic-poisoning*.

Contraindications.—The chief contraindication is gastric irritation. It is generally badly borne, probably on account of impaired digestion, in febrile diseases and in gout.

Administration.—Ordinarily iron should be administered by the mouth and after meals. The least irritant and astringent preparations are the organic compounds, reduced iron, ferrous carbonate, ammonio-ferric citrate and ferric phosphate. The most irritant and astringent preparations are the solution of ferric subsulphate, ferric chlorid, and ferrous sulphate. The

numerous organic compounds of iron with albumin have no great advantages over many of the older inorganic preparations, but they are less injurious to the teeth, less liable to disturb digestion, and are, probably, somewhat more readily absorbed. In exceptional cases iron may be given hypodermically. For this purpose a freely soluble preparation, such as ammonio-ferric citrates, should be selected, and the solution should be dilute (1 mil of a 10 per cent. solution).

Incompatibles.—Ferrous and ferric salts are incompatible with all preparations containing tannin or gallic acid; with ammonia, alkaline carbonates, and mucilage of acacia.

FERRUM REDUCTUM, U. S. P.

(Reduced Iron, Iron by Hydrogen, Quevenne's Iron)

Reduced iron is a fine, grayish-black, insoluble powder, without odor or taste. When pure it is quite free from irritating properties, and, being but feebly astringent, it has little tendency to cause constipation. It is employed only as a *hematinic*. It may be given in doses of from 1 to 5 grains (0.06–0.3 gm.), in pills, capsules, or lozenges.

FERRI CARBONAS

(Iron Carbonate, Green Ferrous Carbonate, FeCO_3)

Iron carbonate is an unstable compound which is readily converted into ferric hydrate on exposure to air. It is not official.

PREPARATIONS

DOSE

Ferri Carbonas Saccharatus, U. S. P. (contains 15 per cent. of freshly precipitated ferrous carbonate, protected from oxidation by sugar).....	5–15 gr. (0.3–1.0 gm.).
Massa Ferri Carbonatis, U. S. P. (Vallet's Mass: about 35 per cent. of ferrous carbonate with sugar and honey).....	3–5 gr. (0.2–0.3 gm.)
Pilulæ Ferri Carbonatis, U. S. P. (Blaud's Pills: each pill contains about 1 gr.—0.06 gm.—of ferrous carbonate, made with granulated ferrous sulphate and potassium carbonate).....	1–3 pills.

Therapeutics.—These preparations are comparatively free from astringency, and are convenient forms in which to administer iron. They are used solely in *anemia*. The saccharated carbonate and the pills of the carbonate (Blaud's pills) are the favorite preparations. The former also should be given in pills or in capsules. Some practitioners prefer Blaud's pills made according to the original formula (equal parts of potassium carbonate and *dried* ferrous sulphate) to those made according to the official formula. The former contain a certain amount of free potassium carbonate.

FERRI CHLORIDUM, U. S. P.

(Ferric Chlorid, Sesquichlorid or Perchlorid of Iron, $\text{Fe}_2\text{Cl}_6 + 12\text{H}_2\text{O}$)

Ferric chlorid occurs in deliquescent, orange-yellow crystalline pieces, having an astringent, chalybeate taste. It is not used internally, but sometimes externally as an astringent or a styptic.

PREPARATIONS

DOSE

Liquor Ferri Chloridi, U. S. P. (contains about 29 per cent. of the crystallized salt)	1-5 min. (0.06-0.3 mil)
Tinctura Ferri Chloridi, U. S. P. (contains about 13 per cent. of anhydrous ferric chlorid, with alcohol, water, and a trace of nitrous ether) . .	5-20 min. (0.3-1.2 mils)
Liquor Ferri et Ammonii Acetatis, U. S. P. (Basham's Mixture: Tincture of ferric chlorid, 4 parts; dilute acetic acid, 6 parts; solution of ammonium acetate, 50 parts; aromatic elixir, 12 parts; glycerin, 12 parts; water, to make 100 parts)	1-4 fl. dr. (4.0-15.0 mils).

Therapeutics.—The solution of ferric chlorid may be used locally as a styptic in controlling bleeding after the *extraction of teeth, removal of tonsils, or application of leeches*. It may occasionally be of service in *hematemesis* and *enterorrhagia*, on account of its local action, but it cannot possibly do good in other internal hemorrhages.

The tincture, in the strength of $\frac{1}{2}$ to 1 fluidram (2.0-4.0 mils) to the ounce (30.0 mils) of water, may be used as an astringent application in *chronic pharyngitis* and *laryngitis*. Ferric chlorid in the form of the tincture or the solution is a useful local remedy in *pharyngeal diphtheria*. It may be prescribed as follows:

℞. Tincturæ ferri chloridi	f ʒj-ij (4.0-11.0 mils)
Glycerini	f ʒss (15.0 mils)
Aquæ	q. s. ad f ʒj (30.0 mils).—M.

Or as Löffler's solution:

℞. Menthol	ʒiiss (10.0 gm.)
Toluol	f ʒx (36.0 mils)
Alcoholis absoluti	f ʒij (60.0 mils)
Liquoris ferri chloridi	f ʒj (4.0 mils).—M.

The tincture is an efficient hematinic in *anemia*, but it is more liable than many of the other preparations of iron to injure the teeth, disturb digestion, and induce constipation. Basham's mixture is a favorite chalybeate diuretic in *chronic nephritis*, but it should be used only when there is anemia, and even then it should be withdrawn if it causes constipation and headache. The tincture has long been regarded as a specific in *erysipelas*.

This claim cannot be substantiated, although the drug seems to be of benefit in some cases. It may be given in doses of from 15 to 20 minims (1.0–1.2 mils) every two or three hours.

Administration.—The tincture of ferric chlorid should be taken after meals, well diluted, through a tube.

Ferrum Dialysatum (*Dialyzed Iron*).—This is an unofficial preparation of the oxychlorid of iron from which acidulous matter has been removed by dialysis. It is a dark-red, tasteless, neutral liquid, quite free from astringency. It is a very unstable compound, and undergoes rapid decomposition in the stomach. It is an extremely feeble chalybeate. The dose is from 10 to 30 minims (0.6–2.0 mils).

FERRI HYDROXIDUM CUM MAGNESIO OXIDO, U. S. P.

(Ferric Hydroxid with Magnesium Oxid, Ferric Hydrate with Magnesia)

This compound is prepared by diluting 40 mils of the solution of ferric sulphate with 125 mils of water and adding this, when needed, to 10 grams of magnesium oxid intimately mixed with 750 mils of water. The Pharmacopœia directs that the diluted solution of ferric sulphate and the magnesia mixture be kept on hand in separate bottles, ready for immediate use, so that the compound may be quickly prepared when needed.

Ferric hydroxid with magnesia is used solely as an antidote in *arsenical poisoning*. It is believed to act by converting the soluble arsenous compounds into insoluble arsenic compounds. It should be given in the dose of 4 fluidounces (120.0 mils) and followed by lavage of the stomach as soon as possible.

FERRI SULPHAS, U. S. P.

(Ferrous Sulphate, Green Vitriol, $\text{FeSO}_4 + 7\text{H}_2\text{Os}$)

Ferrous sulphate occurs as pale, bluish-green, efflorescent prisms having a saline, styptic taste. The dose is from 1 to 5 grains (0.06–0.3 gm.).

PREPARATIONS

DOSE

Ferri Sulphas Exsiccatus, U. S. P.....	1–3 gr. (0.06–0.2 gm.)
Ferri Sulphas Granulatus, U. S. P.....	1–5 gr. (0.06–0.3 gm.).

Therapeutics.—Sulphate of iron is an active astringent. It may be employed as a hematinic in *anemia* attended by relaxation of the bowels. The dried sulphate should be selected for pills.

Crude ferrous sulphate, or copperas, is used as a disinfectant and deodorizer for privies, cess-pools, etc., but its germicidal power is feeble.

FERRI SUBSULPHAS

(Ferric Subsulphate, Basic Ferric Sulphate, Monsel's Salt, $\text{Fe}_2\text{O}(\text{SO}_4)_2$)

Ferric subsulphate is a yellow, hygroscopic, astringent powder, freely soluble in water.

PREPARATION

DOSE

Liquor Ferri Subsulphatis, U. S. P. (Monsel's Solution)..... 3-5 min. (0.2-0.3 mil).

Therapeutics.—Monsel's solution is a prompt and powerful styptic, which is somewhat less irritant in its action than the solution of ferric chlorid. It has been employed chiefly as a *local hemostatic*. When used too freely it produces hard black clots, which may serve to conceal deep-seated hemorrhage.

FERRI IODIDUM

(Ferrous Iodid, Protiodid of Iron, FeI_2)

Ferrous iodid occurs in grayish-white, crystalline masses which are soluble in water with partial decomposition. It is not used in the pure form.

PREPARATIONS

DOSE

Syrupus Ferri Iodidi, U. S. P. (contains 5 per cent. by weight of ferrous iodid)..... 5-60 min. (0.3-4.0 mils)
 Pilulæ Ferri Iodidi, U. S. P. (contain about 1 gr.—0.06 gm.—of ferrous iodid)..... 1-3 pills.

Therapeutics.—Iodid of iron may be employed when it is desirable to combine an alterative with a chalybeate. It is a useful preparation in *tuberculous adenitis*, *syphilitic cachexia*, and *rachitis*. It is usually well tolerated by children, to whom the syrup may be given in doses of from 3 to 20 minims (0.2-1.2 mils), thrice daily, after meals. J. C. Wilson has found large doses of the syrup efficacious in *articular rheumatism* and *other forms of acute arthritis* after failure with salicylic compounds.

As the syrup is injurious to the teeth, it should be taken well diluted, and the mouth should be thoroughly rinsed after its administration.

FERRI CITRAS AND FERRI PHOSPHAS

These compounds are known as the scale preparations, because concentrated solutions of them are spread on plates of glass and allowed to evaporate, so that the salts may be obtained in the form of scales. The following are official:

PREPARATIONS	DOSE
Ferri et Ammonii Citras, U. S. P. (contains 16 per cent. of metallic iron).....	5-10 gr. (0.3-0.6 gm.)
Ferri et Quininæ Citras, U. S. P. (contains 11.5 per cent. of quinin and 13.5 per cent. of metallic iron).....	5-10 gr. (0.3-0.6 gm.)
Ferri Phosphas, U. S. P. (the solubility of this salt is dependent upon the presence of free sodium citrate).....	3-10 gr. (0.2-0.6 gm.).

The phosphate of iron is one of the ingredients of the elixir of iron, quinin and strychnin phosphates (*Elixir Ferri, Quininæ et Strychninæ Phosphatum*), which may be given in the dose of 1 fluidram (4.0 mls).

Therapeutics.—The scale preparations of iron are mild and agreeable *hematinics*. They are comparatively free from astringency, and are usually well borne by the stomach. On account of their solubility they are well adapted for administration in liquid form. When for any reason iron cannot be taken by the mouth the citrate may be given by intramuscular injection. Ampules containing 3 grains (0.2 gm.) are on the market. As a rule, it is sufficient to give the injections every other day.

OTHER IRON SALTS

Ferri Lactas (*Ferrous Lactate*).—This preparation occurs in pale, greenish-white, crystalline crusts, having a slight characteristic odor and a sweetish, ferruginous taste. It is slowly soluble in water. It may be given in doses of from 1 to 5 grains (0.06-0.3 gm.).

Ferri Oxalas (*Ferrous Oxalate*).—This salt occurs as a pale-yellow, odorless, crystalline powder, insoluble in water. It has been lauded by Quinke and by Hayem as a hematinic in *chlorosis*, but it does not seem to have any special advantages. The dose is from 3 to 5 grains (0.2-0.3 gm.).

Ferri Hypophosphis (*Ferric Hypophosphite*).—This salt occurs as a white, odorless, and almost tasteless powder, slightly soluble in water. It has no special advantages. The dose is from 5 to 10 grains (0.3-0.6 gm.). It is contained in the compound syrup of hypophosphites (*Syrupus Hypophosphitum Compositus*), the dose of which is from 1 to 4 fluidrams (4.0-15.0 mls).

Ferri Valeras (*Ferric Valerate*).—This compound is a dark-red, amorphous powder, having the odor of valerian and a mild styptic taste. It may be given with other valerates when a combined chalybeate and anti-spasmodic action is desired. The dose is from 1 to 3 grains (0.06-0.2 gm.).

ORGANIC IRON

Bunge first demonstrated that iron exists in the tissues and in various food-stuffs in the form of a nucleo-albuminate. He subsequently succeeded in separating such a compound from the yolk of eggs, and this he called *hematogen*. The latter differs from ordinary iron salts in being very resistant to the action of sulphids. According to Bunge, inorganic preparations of iron are not absorbed to any extent by the healthy mucous membrane of the alimentary canal, and are useful in anemia only by disposing of the sulphureted hydrogen in the intestine, and thus protecting the food-iron from reduction until its absorption has been accomplished. Recent investigations have proved conclusively that Bunge's view is fallacious, and that inorganic iron compounds are quite capable of absorption and assimilation. Albuminates and peptonates of iron, however, are often better borne by the stomach than the inorganic salts, are less injurious to the teeth, and are, perhaps, somewhat more readily absorbed. Many attempts have been made to produce artificially, and in a way that can be practically utilized, compounds having the characteristics of Bunge's hematogen. Schmiedeberg obtained from pig's liver a compound containing from 6 to 8 per cent. of iron, which he called *ferratin*. Later this preparation was obtained in larger quantities by the action of iron salts on egg-albumen. It is a fine, reddish powder, without odor or taste, insoluble in water, but soluble in dilute alkalis. The dose is from 3 to 10 grains (0.2–0.6 gm.). It may be given in capsules, powders, or tablets, or with milk. *Ovoferrin* is a proprietary preparation made by introducing ferric hydrate into a protein prepared from serum-albumin by electrolysis. Each 100 mls contain the equivalent of 0.4 gm. ($6\frac{1}{2}$ grains) of metallic iron. It is said to be not appreciably affected by the gastric juice. The dose is from 2 to 4 fluidrams (8.0–16.0 mls).

GERMANIUM DIOXID

Recent studies have shown that germanium dioxide causes a marked increase in the number of erythrocytes, with a corresponding rise in the percentage of hemoglobin, but without pronounced increase in the number of leucocytes. Whether the hematinic action depends upon proliferation of the bone-marrow or merely upon stimulation of the erythroblasts to increased activity is not definitely known. Germanium has some features in common with arsenic, but it is much less toxic. Clinically, it has been found of service in some cases of *secondary anemia* and even of *pernicious anemia*, although in the latter its effects have

been only temporary. The exact value of the drug remains to be determined.

Administration may be oral or by subcutaneous injection, but the latter is apparently preferable. For oral administration, doses of $1\frac{1}{2}$ to 3 grains (0.1–0.2 gm.), in 0.2 per cent. solution, may be given daily or every two or three days until 15 grains (1.0 gm.) in all have been taken. A 0.2 per cent. solution can be prepared only by boiling the dioxid in water for several minutes. Precipitation does not occur on cooling. To obtain an unirritating solution for subcutaneous injection the addition of an alkali is necessary. One-half gram of germanium dioxid may be suspended in 122 mls of sterile water and a decinormal solution of sodium hydroxid added drop by drop, with vigorous shaking of the liquid after each addition, until a very faint pink color is produced when a few drops of the solution are treated with a drop or two of a 1 per cent. alcoholic solution of phenolphthalein. Prepared in this way the solution is only slightly irritant, and 5 mls of it correspond to 4 milligrams of germanium dioxid. From 3 to 5 mls may be injected into the buttocks or back at intervals of from 2 to 4 days.

PHOSPHORUS, U. S. P.

(Yellow Phosphorus, P)

Phosphorus is a solid, translucent nearly colorless, non-metallic element obtained from bones. It has a waxy consistence and luster, a peculiar garlicky odor, and a disagreeable taste. By long keeping it turns red, and occasionally black. On exposure it emits white fumes, which are luminous in the dark, and on longer exposure it takes fire spontaneously. It is almost insoluble in water, soluble in 400 parts of absolute alcohol, in 50 parts of fatty oils, and in 17 parts of chloroform. The dose is from $\frac{1}{150}$ to $\frac{1}{50}$ grain (0.0004–0.001 gm.).

PREPARATION

DOSE

Pilulæ Phosphori, U. S. P. (each pill contains $\frac{1}{100}$ gr.—0.0006 gm.)..... 1–2 pills.

Pharmacologic Action.—Unless it is taken in finely divided form or dissolved in oil, phosphorus is absorbed with difficulty. It enters the blood slowly as phosphorus, chiefly in solution in the fatty substances in the intestines, but partly in the form of vapor. Phosphorus vapor it also absorbed by the lungs. While in the tissues it acts as phosphorus. It is excreted in minute quantities by the lungs as phosphorus and also by the kidneys as hypophosphoric acid, and probably as protein compounds.

The drug is an irritant to the mucous membranes, but it is not corrosive. Upon the unbroken skin it has no effect. After absorption its chief effects appear to be upon bone growth, metabolism, and the blood.

Bones.—Wegner found that when phosphorus was given repeatedly in small doses to growing animals it rendered the bones more dense, diminished the cancellous structure, and finally caused narrowing or complete obliteration of the marrow-cavity. These changes were ascribed to stimulation of the bone-forming tissues, and not to the deposition of an excess of phosphates, for in animals fed with phosphorus, but deprived of phosphates, the same hyperplasia occurred in the bones, but the new tissue instead of being hard was gelatinous, as in rickets. These stimulating effects of phosphorus upon the activity of the bone-forming tissues suggested the therapeutic use of the drug in rickets and osteomalacia.

Metabolism.—An important effect of phosphorus in large doses appears to be accelerated autolysis or destructive metabolism in the cells of the various organs of the body. The products of this augmented metabolism are, however, broken down only in part, and in consequence large quantities of intermediary bodies, such as amino-acids, lactic acid, leucin, tyrosin, peptones, etc., appear in the urine. The excretion of nitrogen of phosphates and of sulphur is always greatly increased.

A secondary effect of the accelerated autolytic activity is the appearance of a large amount of fat in the cells of the various organs, particularly the liver, but also in those of the kidneys, heart-muscle, stomach, and bowel. The fat is probably not formed *in situ* from the degeneration of the cell protoplasm itself, as was formerly believed, but transported from other sources in the body and deposited in the affected cells.

Blood.—In therapeutic doses phosphorus tends to increase the number of red blood-cells without, however, augmenting their hemoglobin content. In poisonous doses the drug diminishes the coagulability of the blood. This effect, together with the degenerative changes induced in the endothelial cells of the capillaries, is responsible for the hemorrhagic tendency that occurs in the second stage of phosphorus-poisoning.

Toxicology.—Toxic doses of phosphorus do not usually produce their effects for several hours. The earliest symptoms are intense abdominal pain, persistent vomiting, thirst, a garlicky taste in the mouth, restlessness, and prostration. The ejected material contains mucus, bile, and occasionally disintegrated blood, and may be luminous in the dark. At the end of from twenty-four to thirty-six hours the symptoms gradually

subside and the patient feels comparatively comfortable, but soon the vomiting and pain return, jaundice develops, the liver becomes enlarged and painful, the pulse grows very feeble, and not infrequently ecchymoses appear in the skin and hemorrhages occur from the mucous membranes. The urine is scanty and contains albumin, tube-casts, bile, leucin and tyrosin. In fatal cases death occurs usually in from a few days to two weeks. If the patient recovers the symptoms abate very slowly.

The changes in the organs observed after death are attributable to disturbances of tissue-metabolism and not to the direct irritant action of the drug. The most characteristic feature is wide-spread fatty degeneration of the tissues. The latter is especially marked in the glands of the stomach and intestines, in the liver, kidneys, heart, and muscles. Ecchymoses are found in most of the organs. Areas of complete necrosis are often observed in the stomach and liver. In subacute poisoning the degenerated parenchyma may be replaced in part by newly formed connective tissue.

Treatment.—If the phosphorus has been recently taken, gastric lavage should be practiced at once. Copper sulphate is probably the best emetic, since any excess may serve as an antidote by coating the phosphorus with an insoluble coating of copper. A saline cathartic should be given to remove from the bowel any of the poison that may still be unabsorbed. All oily and fatty matters should be withheld, since they are active solvents of phosphorus. Various oxidizing agents have been employed as chemical antidotes. Potassium permanganate ($\frac{1}{2}$ per cent. aqueous solution) and the solution of hydrogen dioxide are the most useful. Old French oil of turpentine, which is rich in ozone, has been repeatedly recommended, but it cannot be obtained in this country, and ordinary turpentine is useless.

Chronic Phosphorus-poisoning.—Workmen employed in match factories and who are exposed to the fumes of phosphorus develop a symptom-complex to which Magitot has applied the name *phosphorism*. This condition is characterized by anemia, loss of flesh, a garlicky odor of the breath, chronic diarrhea, albuminuria, and, in many instances, necrosis of the maxillary bone ("phossy" jaw). Since phosphorus necrosis occurs chiefly in workmen who have carious teeth, it is usually attributed solely to the local action of the fumes, but there are good reasons for believing that secondary infections contribute largely to its development. It rarely appears, despite the existence of carious teeth, until the worker has been some time, generally many years, at his trade; the sufferer nearly always manifests some of the symptoms of systemic saturation; and finally, Stubenrauch has

demonstrated experimentally that phosphorus fumes exert no direct action on exposed bone or periosteum.

Red or amorphous phosphorus being insoluble in ordinary liquids and non-volatile is free from toxic properties. Phosphoric acid has none of the qualities of phosphorus and acts merely as a mild stomachic. Sodium phosphate is an agreeable laxative. The hypophosphites of calcium, sodium, and potassium are absorbed, but they escape decomposition and are excreted unchanged in the urine. Although they have been extensively employed as tonics, there is no evidence that they are utilized by the tissues. Calcium glycerophosphate is for the most part absorbed and excreted as an inorganic phosphate. Sodium phosphite is extremely poisonous. Sodium pyrophosphate and sodium metaphosphate, when administered hypodermically, paralyze the central nervous system and the heart, and in slow poisoning produce fatty degeneration of the glandular organs and numerous hemorrhagic extravasations.

Therapeutics.—Phosphorus has been employed in *rachitis*, according to Monti, since 1838, but its reputation in this disease is due largely to the very favorable reports of Kassowitz, in Europe, and of Jacobi, in this country. It is not unlikely that much of the benefit which has been observed in rachitic subjects while taking phosphorus has been due in reality to the cod-liver oil, simultaneously administered, and to the improvement in the diet and general hygiene. This view receives some support from the investigations of Zweifel, who found that phosphorus in cod-liver oil is soon converted, through oxidation, into phosphoric acid, and, therefore, loses its peculiar properties. Phosphorus has also been employed with asserted good results in diseases of bones other than rickets, such as *osteomalacia* and *delayed union of fractures*, and in certain functional nervous conditions, such as *neurasthenia*, *melancholia*, *neuralgia*, and *sexual exhaustion*.

Administration.—As phosphorus slowly undergoes oxidation in nearly all menstrua, only freshly made preparations should be prescribed. It may be administered conveniently in the form of the official pills or of an elixir.

Persons vary considerably in their susceptibility to phosphorus, and, therefore, the initial doses should be small, especially in children. Nebelthau has cited an instance in which death occurred in a well-developed child of two years after taking less than $\frac{1}{20}$ grain (0.003 gm.) in the course of sixty hours. Even minute doses sometimes disturb the stomach and excite unpleasant eructations.

Zinci Phosphidum (*Zinc Phosphid*).—This compound appears as a dark-gray, gritty powder, or as crystalline, metallic

fragments having a faint odor and taste of phosphorus. It is insoluble in alcohol or water. The dose is from $\frac{1}{30}$ to $\frac{1}{10}$ grain (0.002–0.006 gm.), in pill. It has been used in the same class of cases as phosphorus, the action of which it is said to resemble.

Acidum Phosphoricum, U. S. P. (*Phosphoric Acid*).—This is a colorless liquid, composed of 85 per cent. by weight of absolute orthophosphoric acid and 15 per cent. of water. It has a strongly acid taste. The dose is from 3 to 5 minims (0.2–0.3 mil), well diluted. Its action is somewhat like that of the dilute mineral acids, and bears no resemblance to that of phosphorus. It may be employed to allay *thirst in diabetes* and *febrile diseases*. It has also been used to *promote gastric digestion*, but for this purpose it is inferior to hydrochloric acid. It is usually prescribed as diluted phosphoric acid (*Acidum Phosphoricum Dilutum*, U. S. P.), the dose of which is from 10 to 60 minims (0.6 to 4.0 mils), in water.

CALCII PHOSPHAS

(Calcium Orthophosphate, $\text{Ca}_3(\text{PO}_4)_2$)

Calcium phosphate is a white, odorless, tasteless, amorphous powder, almost insoluble in water. The dose is from 5 to 30 grains (0.3–2.0 gm.).

PREPARATION

DOSE

Syrupus Calcii Lactophosphatis, U. S. P. (contains about 3 per cent. of the double soluble salt)..... 1–4 fl. dr. (4.0–15.0 mils).

Pharmacologic Action.—The insoluble salts of calcium, of which the phosphate may be taken as a type, produce no important effects upon the system. The greater part resists absorption and reappears in the stools. Even the small portion that enters the circulation is slowly excreted by the intestinal epithelium and the kidneys. In the digestive tract calcium phosphate, like calcium carbonate, acts as a protective and antacid, and probably through its calcium ion, as a depressant to peristalsis. Both the phosphate and the soluble lactophosphate of calcium have been extensively employed in *rachitis* and *osteomalacia*, diseases in which the calcium content of the bone is diminished, and also as tonics in *tuberculosis*, *neurasthenia*, *tardy convalescence* from *acute infections* and *exophthalmic goiter*, but the results have been questionable.

Calcii Glycerophosphas, U. S. P.—This is a fine white powder, odorless and tasteless and soluble in about 50 parts of water. The dose is from 3 to 5 grains (0.2–3 gm.). It is not absorbed as a glycerophosphate, but as an inorganic phosphate,

into which it is transformed in the digestive tract. It is also excreted as an inorganic phosphate. The drug, therefore, has no advantages over the inorganic phosphates, from which the body normally constructs all the organic phosphorus that it requires.

Lecithin.—This is a fatty acid ester of glycerophosphoric acid in combination with cholin, and is one of the forms in which phosphorous occurs in the nervous system, muscles and viscera. The ordinary diet contains sufficient to supply the needs of the system; moreover it has been shown that the organism is quite capable of synthesizing lecithin and other phosphatids from inorganic phosphates. The commercial preparations which are usually isolated from egg-yolk or brain tissue, appear as yellowish or whitish substances of wax-like consistence. The dose is from 1 to 3 grains (0.06–0.2 gm.). When taken by the mouth only a minute portion of the drug is absorbed unchanged, the bulk of being transformed by the pancreatic enzymes into glycerophosphoric or phosphoric acid. It is excreted entirely as an inorganic phosphate. Lecithin has been recommended as a tonic and hematinic, but it is of doubtful value. The usual diet contains more of the compound than is ever prescribed as a medicine.

OLEUM MORRHUÆ, U. S. P.

(Cod-liver Oil)

Cod-liver oil is a fixed oil obtained from the livers of *Gadus morrhua* and other species of *Gadus*. The *shore oil*, or *white oil*, the only variety at present used for medicinal purposes, is extracted by disintegrating the fresh livers with superheated steam, and subsequently straining the resultant pultaceous mass. It is a pale yellow, thin liquid, having a peculiar fishy odor and taste. In addition to olein, palmitin, stearin, and other fatty principles, it contains traces of iodine, bromine, phosphorus, cholesterolin, trimethylamin, and, possibly, bile-salts. The dose is from 1 to 4 fluidrams (4.0–15.0 mls).

PREPARATIONS

DOSE

Emulsum Olei Morrhue, U. S. P. (50 per cent.). 1–8 fl. dr. (4.0–30.0 mls).

Pharmacologic Action and Therapeutics.—Cod-liver oil is a food rather than a medicine. It is superior to other fats, probably because it is more digestible and assimilable. The amount of iodine and of phosphorus present is too small for these ingredients to exert any specific action. It is, however, very rich in the fat-soluble vitamin A, which has an important influence on growth and it contains some other vitamin-like substance which regulates the metabolism of the osseous tissues. The ready

assimilation of cod-liver oil has been attributed by some authorities to the presence of biliary salts; by others, to the presence of a high percentage of free fatty acids, but no explanation that has yet been offered is perfectly satisfactory. In moderate doses cod-liver oil improves the general nutrition, increases the number of red blood-cells, favors the accumulation of fat in the body, and in growing children increases the capacity of the bones to take up or retain calcium. Large doses excite nausea, eructations, vomiting, and diarrhea.

Cod-liver oil, provided it is well borne by the stomach, is of service in a number of conditions in which malnutrition is an important feature. Thus, it is often beneficial in *rickets*, *tuberculosis of the lungs*, *bones or lymph-nodes*, *tertiary syphilis*, *rheumatoid arthritis*, *chronic bronchitis*, and *chronic secondary anemias*. It is especially efficacious in rickets, both as a prophylactic and as a curative remedy. It is often very useful also as a nutrient in the early stages of pulmonary tuberculosis, but it must be given cautiously and withdrawn upon the first evidence of intolerance. When symptoms of secondary infection are prominent, such as fever, sweating, and rapid wasting, it is less likely to be well borne or to do good. In conjunction with general hygienic measures, the prolonged use of cod-liver oil is also of service in preventing the development of tuberculosis in those who show a predisposition to the disease.

Cod-liver oil is rich in a vitamin-like substance which prevents and cures the peculiar condition of the conjunctiva known as *xerophthalmia*.

Contraindications.—High fever and gastric or intestinal irritation are the chief contraindications to its use.

Administration.—Patients who at first have difficulty in taking cod-liver oil may ultimately acquire a tolerance for it if the dose be carefully adapted to their digestive powers. It is well, therefore, to begin with very small doses, even a few minims, and to increase the amount gradually as the stomach becomes accustomed to it. A single dose at bedtime may be well borne when the stomach will not tolerate it during the day. As the oil is digested in the intestine, and not in the stomach, its stay in the latter should be reduced to a minimum, and this can be accomplished by administering it two or three hours after meals. Although it is impossible to disguise completely the fishy odor and taste of cod-liver oil, there are many ways in which the unpleasantness of its administration may be lessened. It may be floated on the surface of porter or root-beer (care being taken to prevent it from touching the glass), and swallowed quickly; it may be taken in tincture of orange-peel, but

perhaps the best way to prescribe it is in soft capsules holding from 10 to 60 minims (0.6–4.0 mls) or in a well-made emulsion. Emulsions containing 50 per cent. of oil may be made with yolk of egg, acacia, or malt extract, and flavored with oil of bitter almond, gaultheria, sassafras, or cinnamon.

℞. Olei morrhuae..... f ℥iv (120.0 mls)
 Olei amygdalæ amaræ..... ℥viii (0.5 ml)
 Acaciæ..... q. s.
 Syrupi..... f ℥ij (60.0 mls)
 Aquæ..... q. s. ad f ℥viij (250.0 mls).—M.
 Sig.—A tablespoonful twice daily, two hours after meals.

Yolk of egg may be used in making the emulsion:

℞. Olei morrhuae..... f ℥viii (250.0 mls)
 Vitelli ovi..... f ℥iss (45.0 mls)
 Glycerini
 Syrupi..... āā f ℥ii (60.0 mls)
 Methylis salicylatis..... f ℥ss (2.0 mls)
 Aquæ..... q. s. ad f ℥xvi (500.0 mls).—M.

The official emulsion is made with acacia and flavored with methyl salicylate. As a rule, children take cod-liver oil readily and even grow to like it. The use of the oil by inunction is unpleasant and of doubtful value.

ALTERATIVES

Alteratives are agents that favorably modify general morbid processes without exerting a pronounced influence on any particular organ. It need scarcely be said that the manner of their action is quite unknown; if it were known, these remedies could be better apportioned among other classes. The term alterative is simply applied for convenience to a group of heterogeneous drugs that experience has shown to be more or less efficacious in certain constitutional diseases, the real nature of which is, in many instances, imperfectly understood. The most important members of this group are:

Arsenic	Colchicum
Iodids	Guaiac
Iodin	Sarsaparilla
Ichthyol	Jambul
Gold and sodium chlorid	Calx sulphurata.

Extracts of endocrinous glands (thyroid, parathyroid, thymus, anterior pituitary lobe, testicle, ovary).

ARSENUM

(Arsenic, As)

Arsenic is not employed for medicinal purposes in the metallic form, but as arsenic trioxid (arsenous acid), as a salt of arsenous acid (an arsenite), as a salt of arsenic acid (an arsenate) or as organic arsenic compounds (sodium cacodylate, sodium arsaniolate, arspenamin).

PREPARATIONS	DOSE
Arseni Trioxidum, U. S. P.	$\frac{1}{60}$ – $\frac{1}{20}$ gr. (0.001–0.003 gm.)
Liquor Acidi Arsenosi, U. S. P. (contains 1 per cent. of arsenic trioxid and 5 per cent. of diluted hydrochloric acid).....	1–5 min. (0.06–0.3 mil)
Liquor Potassii Arsenitis, U. S. P. (Fowler's Solution: contains the equivalent of 1 per cent. of arsenic trioxid and 3 per cent. of compound tincture of lavender) .	1–5 min. (0.06–0.3 mil)
Sodii Arsenas, U. S. P.	$\frac{1}{16}$ – $\frac{1}{8}$ (0.004–0.008 gm.)
Sodii Arsenas Exsiccatus, U. S. P.	$\frac{1}{30}$ – $\frac{1}{12}$ gr. (0.002–0.005 gm.)
Liquor Sodii Arsenatis, U. S. P. (Pearson's Solution; contains 1 per cent. of exsiccated sodium arsenate).....	1–5 min. (0.06–0.3 mil)
Arseni Iodidum, U. S. P.	$\frac{1}{30}$ – $\frac{1}{10}$ gr. (0.002–0.006 gm.)
Liquor Arseni et Hydrargyri Iodidi, U. S. P. (Donovan's Solution: contains 1 per cent. each of arsenous iodid and mercuric iodid).....	1–5 min. (0.06–0.3 mil)
Sodii Cacodylas, U. S. P.	$\frac{1}{2}$ –3 gr. (0.03–0.2 gm.)
Sodii Arsanilas (atoxyl).....	$\frac{1}{3}$ –3 gr. (0.02–0.2 gm.)
Arspenamin (salvarsan).....	3–10 gr. (0.2–0.6 gm.)
Neo-arsphenamin (neo-salvarsan).....	7–14 gr. (0.45–0.9 gm.)

ARSENI TRIOXIDUM, U. S. P.

(Arsenic Trioxid, Arsenous Acid, White Arsenic, As_2O_3)

Arsenic trioxid occurs either as an opaque, white, amorphous powder, or as heavy, amorphous masses of a translucent, glass-like appearance. It has neither odor nor taste. When thrown on hot coals it volatilizes without melting, and emits a strong, garlicky odor. In the presence of water it becomes arsenous acid (H_3AsO_3). It is soluble in from 30 to 80 parts of cold water, slightly soluble in alcohol, and soluble in about 5 parts of glycerin. The dose is from $\frac{1}{60}$ to $\frac{1}{20}$ grain (0.001–0.003 gm.).

Pharmacologic Action.—Local Action.—When applied in concentrated form to mucous membranes and denuded surfaces, arsenic trioxid is a slowly acting and painful caustic. It does not precipitate protoplasm and it is not directly irritant, but it brings about a gradual degeneration and necrosis of the cells,

and at the same time excites an intense inflammatory reaction by paralyzing the capillaries and increasing their permeability. If applied over a large surface, a sufficient quantity may be absorbed to produce systemic poisoning. Toxic amounts may be absorbed also from the intact skin.

Circulation.—An important systemic effect of arsenic in large doses is paralysis or distention of the capillaries, as a result of which the permeability of these vessels is increased, an exudation of serum into the tissues occurs, and all the phenomena of acute inflammation are produced. No matter through which avenue the drug is introduced into the body its paralytic effect on the capillaries is most pronounced in the splanchnic area. It is possible that the favorable influence exerted by small doses of arsenic on growth and nutrition may be due in part to slight changes in the capillaries.

Large doses of arsenic, by paralyzing the capillaries, sooner or later produce edema of the digestive tract and of the skin in various parts of the body, especially about the face. Conjunctivitis, rhinitis and pharyngitis, as well as erythematous or inflammatory skin eruptions, may also result from the same cause. In acute arsenic-poisoning there is a pronounced fall in the arterial bloodpressure, which is brought about chiefly by distention of the capillaries, but partly by depression of the heart-muscle and dilatation of the arterioles. Ecchymoses may also occur as a result of the extreme dilatation of the capillaries and possibly degeneration of the capillary endothelium.

Blood.—In health arsenic has little or no effect upon the blood, but in certain forms of anemia, especially pernicious anemia, it may increase decidedly the number of erythrocytes. The view that the blood improvement is due to stimulation of the bone-marrow receives some support from the researches of Stockman and Grieg, who found that arsenic increased the vascularity of the marrow and led to a replacement of fat by red corpuscles. In chronic arsenic-poisoning cell destruction predominates over cell regeneration, and in consequence of this effect upon the marrow-cells and the red blood-corpuscles themselves there may be profound anemia.

Metabolism.—Therapeutic doses of arsenic have a favorable influence upon growth and nutrition. Whether this is the result of a direct stimulant action on the cells themselves or of dilatation of the blood and lymph capillaries is not known. The epithelial tissue of the skin appears to be especially susceptible to the regenerating effect of the drug. Toxic doses of arsenic have an opposite effect, that is they tend to increase tissue destruction and to inhibit the function of the various organs. An important

autopsy finding in poisoning is extensive fatty degeneration of the cells of the liver, kidneys, intestines, muscles, heart and bloodvessels. Clinical experience seems to show that the cells of pathologic new growths are somewhat more sensitive to the disintegrating effects of arsenic than the cells of normal tissues.

Nervous System.—The central nervous system apparently shares in the improvement of general nutrition that is effected by small doses of arsenic. In frogs toxic doses of arsenic cause a rapid paralysis, which is probably of central origin. In man nervous phenomena occur in both acute and chronic poisoning, but they are especially pronounced in the latter. The paralysis of chronic poisoning is, as a rule, the result of a polyneuritis, similar to that produced by various other toxic agents; in a few cases, however, paralysis of spinal origin has been observed.

Alimentary Canal.—In minute doses arsenic improves the appetite and probably increases gastric secretion. Large doses produce inflammatory changes in the mucous membrane with colicky pains, vomiting and diarrhea. Jaundice is not uncommon in arsenic-poisoning, especially the chronic form. It may be due to compression of the bile-ducts by the swollen fatty cells of the liver or to abnormal destruction of the red blood-cells.

Kidneys.—Therapeutic doses of arsenic, unless the administration is long continued are without effect. Toxic doses, and even moderate doses in the course of time, produce nephritis, either of a vascular or tubular type. As a rule, the vascular changes predominate.

Excretion.—This occurs chiefly by the urine and feces, but partly also by the milk, sweat, saliva, etc. After administration by the mouth the bulk of the drug escapes in the feces, and after subcutaneous injection the largest amount is excreted in the urine. Arsenic leaves the body very slowly, traces often being found in the secretions for weeks after its administration has been suspended. Owing to its slow elimination, arsenic has a tendency when given over long periods, even in small amounts, to accumulate in the body and to produce chronic poisoning.

Action on Lower Organisms.—While arsenic has comparatively little bactericidal power, it is decidedly toxic to certain protozoan parasites. This is particularly true of the organic compounds after they have been acted upon by the tissues.

Toxicology.—**Acute arsenical poisoning** is usually suicidal or accidental and is due, as a rule, to white arsenic (arsenic trioxid) or to Paris-green (aceto-arsenite of copper). It is characterized by severe abdominal pains, persistent vomiting, profuse diarrhea with "rice-water" stools, great thirst, oliguria, muscular cramps,

cyanosis, and collapse. Death, which usually occurs in from twenty-four hours to three days, is often preceded by delirium, convulsions, and coma. If recovery ensues, the symptoms of acute poisoning may be slowly replaced by those of chronic poisoning. Occasionally cases are encountered which depart somewhat from the usual type; thus, there may be a rapid termination in collapse or coma without any pronounced abdominal symptoms; sometimes a temporary remission in the symptoms occurs about the third day, and this is followed, as in the case of phosphorus-poisoning, by jaundice, delirium and coma; again, there may be in addition to the gastrointestinal symptoms, an extensive urticarial or vesiculo-papular rash. It is difficult to fix upon the minimum fatal dose of arsenic trioxid, since much that is ingested may escape absorption. According to Taylor, about 2 grains (0.13 gm.) is the minimum fatal dose for an adult, but cases are on record in which much larger amounts have been swallowed without destroying life. Apparently, the finer the particles of a preparation, the greater is its toxicity.

After death the chief macroscopic changes are found in the alimentary canal. A large quantity of serous fluid is usually present, the intestine itself is edematous, and the epithelial covering is more or less exfoliated. There is, however, no pronounced corrosion of the tissues. Microscopic examination reveals fatty changes in the intestinal epithelium and in the liver, kidneys, heart and muscles.

Treatment of Acute Poisoning.—Ferric hydroxid with magnesia (see p. 301), administered while still moist, in doses of 3 or 4 ounces (90.0–120.0 mls), is recommended as a chemical antidote. It forms with arsenous acid an arsenate of iron, which has been supposed to be only slightly toxic. However, recent investigations have thrown considerable doubt upon the efficacy of this treatment. Whether the antidote is given or not, the stomach should be emptied promptly by means of the stomach-pump or by an emetic. Unless diarrhea has already developed, a solution of magnesium sulphate should be given to remove any of the poison that may have passed from the stomach to the bowel. Mucilaginous drinks, bismuth subcarbonate, and morphin may be employed to relieve abdominal pain and diarrhea. Saline transfusion may be of service in combating dehydration and the tendency to collapse.

Chronic arsenical poisoning may be a sequel of acute poisoning, may follow the prolonged use of the drug for medicinal purposes, may result from the use of foods or liquors contaminated with arsenic, may be produced by the constant inhalation of dust arising from wall-papers, furs, artificial flowers or other fabrics

containing arsenic, or may be acquired by workers who handle arsenic or who are exposed to arsenical fumes. It may be manifested by gastro-enteritis, catarrh of the upper air passages, anemia, peripheral neuritis, and various rashes of an erythematous or inflammatory type. Pigmentation of the skin has also been observed. Polyneuritis is occasionally seen in children to whom the drug is being given for chorea. Railton has reported four cases in which the paralytic phenomena did not appear until from 1 to 3 weeks after the drug had been discontinued. In 1900 more than 3000 cases of poisoning occurred in England from drinking beer containing $\frac{1}{4}$ to $\frac{3}{4}$ grain (0.01–0.02 gm.) per gallon. The arsenic was traced to the sulphuric acid which was made from arsenical pyrites and which was used in producing the glucose employed in the brewing. In this epidemic gastro-intestinal symptoms were not marked, the chief manifestations being numbness and tingling in the hands and feet; a sense of burning in the feet and painful flushing, resembling erythromelalgia; and certain cutaneous lesions, consisting of melanosis, herpes zoster, hyperidrosis, hyperkeratosis of the palms and soles, and pemphigoid eruptions.

In addition to causing hyperkeratosis of the hands and feet, prolonged arsenical medication may result in other lesions of the skin indicative of increased cellular proliferation. Thus, it may lead to horny growths, multiple warts and, perhaps epithelioma. In 1899 Hartzell collected 11 cases of epithelioma occurring in psoriasis and apparently due to the prolonged use of arsenic.

Treatment of Chronic Poisoning.—The indications are to prevent the further absorption of arsenic, to favor elimination, and to improve the general nutrition. Potassium iodid has been recommended, but it is of doubtful value. The treatment of arsenical neuritis does not differ from that employed in other forms of toxic neuritis.

Tolerance.—Under certain conditions, which are not well understood, the prolonged use of arsenic, instead of causing chronic poisoning, may result in the establishment of a tolerance for the drug. In some parts of Austria it is a custom among many of the peasants to take gradually increasing doses of arsenic, under the belief that it improves the complexion and increases the endurance. According to Knappe, as much as 5 or 6 grains (0.3–0.4 gm.) are sometimes taken at a single dose without harm. The practice, however, even among these peasants, is not altogether free from risk; and in other countries it is the exception, rather than the rule, for the continued administration of arsenic not to be followed by untoward effects. Immunity from symptoms in habituated persons has been attributed to

the development of changes in the alimentary canal which render it more impervious to the poison.

Therapeutics.—Locally, arsenic trioxid has been used with some success as a caustic in removing from the skin circumscribed, superficial new growths, such as *lupus* and *epithelioma*, especially the latter. For this purpose a paste made by adding equal parts of the trioxid and acacia to a saturated solution of cocain hydrochlorid is used. This should be spread over the diseased surface, and allowed to remain for from twenty-four to forty-eight hours, when a poultice may be applied to remove the slough. It is inadvisable to spread the paste over a larger area than a square inch at one time. Arsenic is used also by dentists to *destroy the nerves of teeth*.

Internally, arsenic is employed empirically in a number of diverse conditions. Next to iron it is the most effective drug we have in *anemia*. Even in *pernicious anemia* marked improvement is often observed under its use. A good plan is to begin with 2 drops of Fowler's solution, three times a day, after meals, and to increase the dose by 1 drop daily until 10 or even 15 drops are taken at each dose. After continuing for a week with the maximum dose, it is advisable to suspend the treatment for a few days and then to resume it with 5 or 6 drop doses and to increase the amount gradually as before. Of course, if ill-effects occur the drug must be discontinued altogether for a time. Arsenic in the form of Fowler's solution is apparently useful in *Sydenham's chorea* or *St. Vitus's dance*, although it must be used with caution, and upon the occurrence of puffiness below the eyes, conjunctivitis, epigastric pain or diarrhea its administration should at once be suspended. *Neuralgia* the result of anemia is not rarely benefited by arsenic. As an alterative, it is sometimes of service in *leukemia*, *Hodgkin's disease*, *chronic tuberculosis*, *rheumatoid arthritis* and *chronic gout*. In *bronchial asthma* it seems at times to do good, although it is even less reliable than potassium iodid. According to Murray, it is especially useful in the asthma of children and of old emphysematous persons.

Both Bramwell and Balfour have spoken favorably of the prolonged use of arsenic ($\frac{1}{100}$ – $\frac{1}{50}$ grain—0.0006–0.0012 gm.) in the less severe forms of *chronic myocardial disease*. In these cases it may often be combined advantageously with strychnin.

In *malaria* it is a useful adjuvant to quinin. In the form and doses ordinarily employed, it probably has no destructive influence on the parasite, but when employed after the subsidence of the paroxysms, it proves a valuable blood restorer.

The administration of arsenic often gives gratifying results in

certain chronic skin diseases of a sluggish type. It is especially useful in *psoriasis* and *chronic squamous* and *papular eczema*. The drug is contraindicated when the inflammatory process is of an acute or active type. Administered in increasing doses until the limit of tolerance is reached, it is often of considerable value also in *pemphigus*. It is common practice to give Fowler's solution in conjunction with bromids to prevent the latter from causing *acne*.

Administration.—As persons vary considerably in their susceptibility to the action of arsenic, it is always well to begin with small doses of the drug and to increase them gradually. Puffiness under the eyes, especially noticeable in the morning, and looseness of the bowels, with colicky pains, are the usual indications of saturation. For pills, arsenic trioxid is generally selected, and for solutions, the solution of potassium arsenite. When a very decided impression is desired, as in chorea and pernicious anemia, the best preparation to employ is Fowler's solution,* and this should be prescribed by itself, so that changes in the doses may be readily made from day to day. When arsenic is prescribed for its constitutional effect, it should be given after meals. When it is not tolerated by the stomach, it may be given subcutaneously in the form of sodium arsenate or sodium cacodylate.

The following formulæ will illustrate the manner of prescribing the drug in combination:

R_x. Arseni trioxidi..... gr. ss (0.03 gm.)
 Quininæ sulphatis..... gr. l (3.2 gm.)
 Ferri reducti..... gr. xl (2.6 gm.)
 Pulveris capsici..... gr. x (0.65 gm.).—M.
 Fiant pilulæ No. xx.
 Sig.—One after meals. (*Malaria after the arrest of the paroxysms.*)

R_x. Arseni trioxidi..... gr. ss (0.03 gm.)
 Extracti nucis vomicæ..... gr. vi (0.4 gm.)
 Massæ ferri carbonatis..... ʒiiss (6.0 gm.).—M.
 Fiant pilulæ No. xxx.
 Sig.—One pill after meals.

Incompatibles.—Salts of iron, silver, copper, and ammonium, magnesia, lime and tannic acid.

Arseni Iodidum, U. S. P.—Iodid of arsenic occurs in orange-red, glossy crystals, having the odor and taste of iodine. It is soluble in water and alcohol. The dose is from $\frac{1}{30}$ to $\frac{1}{10}$ grain (0.002–0.006 gm.). It has been found useful in *tuberculous adenitis*. Saint-Phillippe has employed it with success in the troublesome *bronchitis* of strumous children. He recommends

* Introduced by the English clinician, Thomas Fowler in 1786.

5 minims (0.3 mil) of a 1 per cent. solution, gradually increased to 10 to 15 minims (0.6–1.0 mil), with meals.

Aqueous solutions should be freshly prepared and kept in a cool place, since they are prone to decompose into arsenous and hydriodic acids.

SODII CACODYLAS, U. S. P.

(Sodium Cacodylate; $(\text{CH}_3)_2\text{AsO.ONa} + 3\text{H}_2\text{O}$)

Sodium cacodylate is the sodium salt of cacodylic acid, or dimethyl arsenic. It is a white, deliquescent, tasteless powder, readily soluble in water. Its actions are qualitatively similar to those of inorganic arsenic, but like other organic compounds of arsenic it is reduced slowly to ionic form in the body and is, therefore, less irritant and less toxic. When administered by the mouth it gives a garlicky odor to the breath. It is best given hypodermically or intramuscularly in doses of from $\frac{1}{2}$ to 2 grains (0.03–0.13 gm.) daily. When taken by the mouth cacodylates may become poisonous by meeting with reducing agents in the alimentary canal. Murrell has reported a case of poisoning in a tuberculous patient from the administration of sodium cacodylate by the mouth in doses of 1 grain (0.065 gm.) twice daily. The toxic symptoms appeared after the eleventh dose.

Sodium cacodylate may be used in the same conditions in which the inorganic compounds of arsenic are efficacious. It may be given the preference when for any reason the latter are not well borne and a persistent arsenic effect is desired. It has been found more or less efficient in *pernicious anemia*, *leukemia* and *Hodgkin's disease*.

SODII ARSANILAS

(Sodium Arsanilate, Atoxyl, $\text{C}_6\text{H}_4(\text{NH})_2.\text{AsO.OH.O Na} + 3\text{H}_2\text{O}$)

Sodium arsanilate is sodium arsenate with one hydroxyl group replaced by anilin. It is a white powder soluble in about 6 parts of water. Single doses are much less irritant and much less toxic than single doses of inorganic arsenic, but when given in large doses the drug is prone to produce degeneration of the optic nerve and blindness. Koch found that eye symptoms did not occur with doses less than $7\frac{1}{2}$ grains (0.5 gm.).

Atoxyl has been found effective in the treatment of various protozoal affections, but owing to its tendency to cause blindness it has been largely supplanted by arsphenamin. In *trypanosomiasis*, or *sleeping sickness*, however, it is apparently superior to arsphenamin, especially when used in conjunction with intravenous injections of tartar emetic.

The dose of atoxyl is 3 grains (0.2 gm.) in 15 mls of distilled water intramuscularly every third day, cautiously increased to 6 or 7 grains (0.4–0.45 gm.).

ARSPHENAMIN

(Salvarsan, Arsenobenzol, "606," Diamino-dihydroxyl-arsenobenzol-hydrochlorid, $C_6H_3As.OH.NH_2HCl + 2H_2OC_6H_3As.OH.NH_2HCl + 2H_2O$)

Arsphenamin is a fine yellow, crystalline powder, readily soluble in water. It contains 31.6 per cent. of arsenic. As it is readily oxidized, it is kept in ampules in a vacuum. The dose is from 3 to 10 grains (0.2–0.6 gm.) intravenously.

Pharmacologic Action and Therapeutics.—Arsphenamin is not very destructive to bacteria *in vitro*, but when introduced into living animals it is exceedingly effective in freeing the tissues of the spirochetes of syphilis, of relapsing fever, and of yaws and certain other protozoa, being more damaging to these parasites than to the tissues of their host. As the drug is much more effective in the blood than *in vitro* it is probable, as Ehrlich believed, that its influence is indirect rather than direct, and of the nature of a complement-fixation reaction.

Locally, arsphenamin is very irritant. As some of its irritant properties are due to its strongly acid reaction, it is always administered in neutral suspension or in alkaline solution. The systemic effects of toxic doses are mainly those of arsenic. Of the various untoward reactions that sometimes result from the use of the drug in therapeutic doses, however, some appear to be due to decomposition of the compound, others to the liberation in the tissues of large amounts of spirochetal endotoxins and others, still, to anaphylaxis, the patient after repeated injections becoming sensitized to a new protein produced by the union of arsphenamin with the blood serum (Draper).

Arsphenamin undergoes decomposition in the body and is excreted chiefly in the urine and feces as ionized arsenic. Excretion begins promptly, but proceeds somewhat slowly, and frequently traces of arsenic may be found in the urine after several weeks.

Arsphenamin is a valuable remedy in *syphilis*, equal to and often surpassing mercury in effectiveness. It is useful in all stages of the disease, but, in general, the earlier it is used the greater is its curative power. In the primary stage repeated injections rapidly sterilize the surface lesions and not rarely eradicate completely the systemic infection. In the later stages, although as a rule it promptly removes the symptoms, it often fails to effect a complete cure unless supplemented by mercury. Fournier and Guenot, Lacapère and Laurent, Michel

and Goodman report favorably on the abortion of syphilis by the use of moderate doses of arsphenamin during the primary incubation period.

The dose of the drug and the frequency of its administration vary with the stage of the disease, the general health of the patient, the age and the sex. In florid syphilis in robust men a full dose, 10 grains (0.6 gm.), should be given once a week, or even every third or fourth day, until at least six doses in all have been given, and then a course of mercurial injections or other mercurial treatment should be carried out over a period of 6 or 8 weeks. In latent and tertiary syphilis several courses of arsenic and mercury are usually necessary. For less robust men and for women the dose should be from 4 to 8 grains (0.25–0.5 gm.), and for children, 2 to 5 grains (0.13–0.3 gm.). The drug should be given with at least 120 mls of saline solution for each 10 grains (0.6 gm.), and introduced into the vein, preferably one at the elbow, from a gravity buret. In preparing the saline solution only freshly distilled water should be used. The arsphenamin should first be dissolved in about 50 mls of hot saline solution and then alkalinized with sodium hydroxid (4 drops of a 15 per cent. solution per 0.1 gm.), the latter being added a drop at a time and the solution well shaken after each drop until the fluid becomes clear. Finally, enough cold saline solution should be added to bring the total amount up to 120 mls. The solution should be used at once after it is made. Not less than 5 minutes should be allowed for the 120 mls to enter the vein. The patient should be recumbent during the treatment and should remain so for several hours after it.

Intramuscular injections of arsphenamin have been used, but they are objectionable, being painful, being attended with much more danger of necrosis, and being less certain in their effects than intravenous injections.

Intraspinal injections of arsphenaminized serum, following the technic of Swift and Ellis, have given encouraging results in cerebrospinal syphilis and even in some early cases of locomotor ataxia and parietic dementia. The patient is given the drug intravenously in the usual way, and an hour later 60 mls of blood are withdrawn by venepuncture. The serum of this blood, after being diluted with normal saline to form a 40 per cent. mixture, is heated to 56° C. for $\frac{1}{2}$ hour and then kept on ice. Later in the day a lumbar puncture is made and an amount of fluid equivalent to the amount to be introduced is withdrawn. While the needle is still in place 30 or 35 mls of the diluted arsphenaminized serum are allowed to flow into the subarachnoid space by gravity through a rubber tube (40 cm. in length) connected to

the barrel of a Luer syringe. After the treatment the patient should be kept in bed with his feet slightly elevated for 24 hours. Untoward symptoms, such as headache, pains in the legs, and vesical disturbances, are sometimes noted. The treatment, if well borne, is repeated at intervals of from 10 days to 2 weeks and for 4 to 6 administrations, according to the patient's tolerance.

Untoward Effects of Arsphenamin.—Not infrequently the injections are followed in a few hours by lumbar pains, chills, fever, nausea and vomiting. These effects usually subside within 24 or 36 hours and are not serious. In another and much smaller group of cases the symptoms occur after 2 or 3 days and consist of headache, vomiting, extreme weakness, albuminuria, and oliguria or actual suppression of urine. Jaundice may also develop and coma may supervene. Death may result from collapse, uremia, or hemorrhagic encephalitis.

In other cases a reaction, apparently of an anaphylactic nature, occurs within a few minutes after the second injection or a later one and is characterized by a sense of suffocation, flushing of the face or cyanosis, and sometimes chill, fever, and an urticarial or a diffuse erythematous eruption. On account of the resemblance of the symptoms in many cases to nitrite-poisoning, reactions of this type have been designated *nitritoid* reactions.

Not rarely, probably as a result of the liberation of a large amount of luetic toxin, the syphilitic eruption is temporarily intensified by the injection (Jarisch-Herxheimer reaction). Occasionally, arsphenamin injections are followed after an interval of several weeks by neuritis, but whether this condition is the result of the medication or of the syphilis itself is not known with certainty. The acoustic nerve is most often involved, but other nerves, including the optic nerves, may be attacked.

Locally, intravenous injections may be followed by phlebitis, and intramuscular injections by abscess and sloughing.

Contraindications.—The chief contraindications are acute febrile diseases of all kinds, advanced pulmonary tuberculosis, chronic alcoholism, and severe nephritis not due to syphilis, and marked idiosyncrasy to arsenic. The drug must be used with caution in the presence of severe disease of the circulatory organs, acute cerebral syphilis, advanced degenerative lesions of the central nervous system, and affections of the optic and auditory nerves.

Use of Arsphenamin in Conditions Other than Syphilis. Aside from syphilis, arsphenamin has proved successful in *yaws* or *frambesia*, *relapsing fever* and *Vincent's angina*. It has been found to be more or less serviceable also in *kala-azar*, *refractory malaria*, *filariasis* and *sleeping sickness*, as well as in a

number of conditions in which the ordinary forms of arsenic are usually employed, such as *pernicious anemia*, *leukemia* and *splenic anemia*.

Neoarsphenamin.—This compound is sodium-diamino-dihydroxy-arseno-benzol-methanol-sulphoxylate mixed with inert inorganic salts. It is an orange-yellow powder, of neutral reaction, dissolving readily in cold water. It contains about two-thirds as much arsenic (20 per cent.) as arsphenamin. It is much more unstable than arsphenamin, and like the latter is marketed only in glass ampules containing the required dose. Even in this form it gradually decomposes. The dose for an adult is from 7 to 14 grains (0.45–0.9 gm.); for a child of 10 years, $2\frac{1}{2}$ to 5 grains (0.15–0.3 gm.). Solutions may be given intravenously or intramuscularly. But a single ampule should be dissolved at a time. Compared with arsphenamin, neoarsphenamin dissolves almost immediately in water, does not require neutralization with sodium hydroxid and is distinctly less toxic. Moreover, solutions of neoarsphenamin may be administered through much smaller needles than those of arsphenamin, thus causing the patient less pain. On the other hand, neoarsphenamin is about one-third less efficient in syphilis than arsphenamin.

Administration.—Solutions of neoarsphenamin may be administered intravenously from a buret by the gravity method or directly from a Luer syringe, without the intervention of rubber tubing or any other apparatus. For intramuscular injections a Luer syringe should be used, with a needle from $1\frac{1}{2}$ to 2 inches long, so that the drug may be injected into the muscles and not into the subcutaneous tissues. The injections are best made into the buttocks. To prevent pain when the drug is given intramuscularly, it is advisable to inject beforehand 2 or 3 mls of a 1 per cent. solution of procain (novocain). For intravenous injections the drug should be dissolved, with but slight agitation, in from 50 to 20 mls of freshly distilled, slightly warm (*not hot*) sterilized water. Unless the solution is brilliantly clear it should be rejected, as cloudy solutions invariably cause severe reactions. For intramuscular injection about 3 mls of freshly distilled water should be used for each $2\frac{1}{2}$ grains (0.15 gm.) of neoarsphenamin. Patients should not receive intravenous or intramuscular injections immediately after a meal and should rest quietly for several hours after the treatment. The injections may be given at intervals of from two days to a week.

Silver Arsphenamin.—This is the sodium salt of silver-diamino-dihydroxy-arseno-benzol. It contains about 20 per cent. of arsenic and about 15 per cent. of silver, and appears

as a brownish-black powder, unstable in the air, and readily soluble in water. It has been recommended for the same conditions in which arsphenamin and neoarsphenamin have proved useful, but it apparently has no advantages over the latter, and, moreover, is capable of producing argyria. In Lochte's case permanent discoloration of the skin appeared within 5 days after the intramuscular injection of a single dose of 0.2 gm.

The dose of silver arsphenamin is from 2 grains (0.13 gm.) to 5 grains (0.3 gm.) in male adults or to 3 grains (0.2 gm.) in female adults.

POTASSII IODIDUM, U. S. P.

(Potassium Iodid, KI)

Potassium iodid occurs as colorless, transparent or translucent crystals, or as a white granular powder, having a pungent, saline taste. It is soluble in 0.7 part of water, 2 parts of glycerin, or 22 parts of alcohol. The usual dose is from 5 to 10 grains (0.3–0.65 gm.), well diluted, thrice daily; but in syphilis often three or four times this amount may be given with advantage.

PREPARATIONS

DOSE

Liquor Iodi Compositus, U. S. P. (Lugol's Solution: contains 10 per cent. of potass. iodid and 5 per cent. of iodin).....	1–5 min. (0.06–0.3 mil)
Tinctura Iodi, U. S. P. (5 per cent. of potass. iodid and 7 per cent. of iodin).....	1–3 min. (0.06–0.2 mil)
Unguentum Iodi, U. S. P. (4 per cent. of potass. iodid and 4 per cent. of iodin)	

Pharmacologic Action.—In health moderate doses of potassium iodid produce no demonstrable effects beyond a slight increase in the secretion of mucus and of urine and, perhaps, some disturbance of the stomach. The drug is rapidly absorbed from all parts of the digestive tract, and reappears in the secretions in less than fifteen minutes after its ingestion. The larger portion is eliminated through the kidneys, but small quantities escape in the saliva, tears, milk, and perspiration. While the bulk of the drug escapes from the body within a few hours, a small portion is retained for a time and is then excreted somewhat slowly, consequently continuous administration sooner or later results in cumulation. Bromids and chlorids hasten the excretion of iodids. A portion of the retained iodid is stored up as thyroxin in the thyroid gland, the functional activity of which is thereby increased.

Large doses of potassium iodid cause burning in the stomach, nausea, vomiting, and diarrhea. The continuous use of the drug is followed, after a variable time, by a group of symptoms

known as *iodism*. This condition has been attributed to the irritant effects of free iodine, but there is no evidence to support this assumption. Its manifestations are most commonly associated with the mucous membrane of the respiratory tract and with the skin, and consist of frontal headache, lacrimation, running at the nose, sneezing, soreness of the throat, cough, an increased flow of saliva, and, later, of a generalized acneiform eruption on the skin. More rarely the eruption is of an erythematous, purpuric, or bullous character. Parotitis and intense dyspnea from inflammatory edema of the larynx have occasionally been observed. In some instances symptoms suggesting Graves' disease have developed, such as tremors, cardiac palpitation, sweating, and loss of weight. It is not improbable that the last-named symptoms owe their origin to an influence exerted by the iodine on the thyroid gland. Profound cachexia, loss of sexual power, and atrophy of the mammae or testicles have also been reported as resulting from the prolonged use of iodides. The amount of the drug required to induce iodism varies considerably in different subjects. Daily doses of 2 or 3 drams (8.0–12.0 gm.) are sometimes well borne, and, on the other hand, doses of from 2 to 3 grains (0.13–0.2 gm.) a day may soon produce unpleasant symptoms. Russell has reported a case in which 5 doses of 4 minims (0.25 mil) of the syrup of ferrous iodide with 2 grains (0.13 gm.) of potassium iodide, over a period of three days, caused acute iodism with fatal termination in a man of 68 years, suffering from rheumatoid arthritis. Patients with chronic nephritis are, as a rule, especially intolerant. Syphilis does not necessarily confer immunity to iodism.

In syphilis, actinomycosis, tuberculosis, and similar infectious granulomata, iodides have the important property of hastening the liquefaction and absorption of the necrotic tissue, but the manner of their action is not known. It has been suggested, however, that they may act by binding the antitrypsin, thus leaving the tryptic or proteolytic ferments unopposed (Jobling and Petersen). While the iodides are apparently without germicidal power when administered internally, they are, nevertheless, of considerable value in syphilis, since they tend to disintegrate the granulomatous formations and thus to give arsenic and mercury ready access to the spirochetes. On the other hand, in tuberculosis their solvent action is disadvantageous, since in this disease we have at present no direct means of destroying the specific organisms, which having been set free by the iodides, have more power to disseminate the infection.

Therapeutics.—The best effects of potassium iodide and other iodides are observed in the *later stages of syphilis*, especially when

the periosteum, the bones, the deeper parts of the skin, the connective tissue, the blood vessels, the central nervous system or the viscera are the seat of guminatous infiltrations. The drug is in no sense a substitute for mercury or arsphenamin, but when used in conjunction with these remedies it aids materially in removing the lesions. No benefit is to be expected from the administration of iodids in the degenerative form of nervous syphilis, as exemplified by locomotor ataxia, except, possibly, in the earliest stages of these disorders; nor are the iodids of value in primary or secondary syphilis, unless, as is rarely the case, the lesions are of the precocious type. The dosage in syphilis is from 5 to 10 grains (0.3–0.6 gm.), three times a day, gradually increased to 30 or 40 grains (2.0–2.6 gm.), or, if necessary, even to 60 grains (4.0 gm.) three times a day.

In doses of 2 or 3 drams (8.0–12.0 gm.) daily, over long periods, it seems to be of value also in *actinomycosis*, and it should be used in all cases irrespective of other forms of treatment.

In certain diseases involving the blood vessels, especially *premature arteriosclerosis*, *essential arterial hypertension*, *aneurysm of the aorta*, and *angina pectoris*, the iodids often do good, although the manner of their action is not definitely known. They are said to act by lessening the viscosity of the blood, but this is doubtful. They certainly do not cause general arterial dilatation. To be effectual, daily doses of from 30 to 40 grains (2.0–2.6 gm.) should be given for several months. In aneurysm, even if the iodids do not retard the progress of the disease, they frequently lessen the pain. In angina pectoris they are more effective in preventing the recurrence of the attacks than other remedy, except the nitrites. According to Osler, the patients who improve the most are the robust, middle-aged men, in whom angina is the sole symptom. In the senile type of arteriosclerosis iodids are useless.

In some cases of *subacute* and *chronic arthritis*, whether *rheumatoid* or *gouty*, iodids are beneficial. They are often prescribed to promote absorption of the effusion in *serofibrinous pleurisy* and *pericarditis*, but in these conditions they usually fail. In so-called *essential asthma* and in *chronic bronchitis*, when the sputum consists chiefly of thick, viscid mucus, iodids may sometimes be of service.

It has recently been demonstrated that the administration of an iodid in doses of 3 grains (0.2 gm.) daily for 10 consecutive days, twice a year, is effectual in *preventing simple goiter* in adolescence. It is well recognized, also, that small doses of iodid, 1 or 2 grains (0.06–0.13 gm.) a day, over a long period, exert a curative influence on the simple goiter of young persons.

In hyperthyroidism and exophthalmic goiter iodids should be avoided.

In *chronic metallic poisoning*, especially by lead or mercury, potassium iodid is apparently efficacious, although the manner of its action is not known.

Administration.—Individual susceptibility to the iodids varies remarkably, and idiosyncrasies are frequently encountered. Children usually bear the drug better than adults. The initial dose should always be small, and the amount gradually increased as the tolerance of the patient permits. No drug is of much value in preventing iodism when the tendency to it is pronounced, but the tincture of belladonna, in doses of from 3 to 5 minims (0.2–0.3 mil) and calcium lactate in daily doses of 1 dram (4.0 gm.) will sometimes relieve the catarrhal symptoms, and Fowler's solution, in doses of 2 or 3 minims (0.1–0.2 mil), the acne. Iodids should be given after meals and in dilute solution. The unpleasant taste may be disguised with compound syrup of sarsaparilla. A convenient method of prescribing potassium iodid is in the form saturated aqueous solution, so prepared that 1 minim (0.06 mil) will contain 1 grain (0.065 gm.) of the salt. As prescribing the iodid and water, ounce for ounce, results in a solution weaker than the one indicated, Hynson suggests the following plan: Dissolve 480 grains (31.1 gm.) of the salt in 5½ drams (20.34 mls) of hot water, and then make up the solution to 8 drams (29.57 mls) with water. This results in a solution containing 1 grain (0.065 gm.) to a minim (0.06 mil). A drop from a medicine dropper will contain a little less than 1 grain (0.065 gm.). If taken in milk, most patients do not find the solution disagreeable. When not tolerated by the stomach, potassium iodid may be given as an enema in milk or by drop proctoclysis.

Incompatibles.—Mineral acids and salts, alkaloids, and spirit of nitrous ether. Potassium iodid is often added in excess to solutions of corrosive sublimate to form the soluble double iodid of mercury and potassium.

SODII IODIDUM, U. S. P.

(Sodium Iodid, NaI)

Sodium iodid occurs in colorless, cubical crystals or white crystalline powder, of a bitter, saline taste. On exposure to moist air it deliquesces and liberates free iodine. It is soluble in 0.5 part of water or in 2 parts of alcohol. The dose is from 5 to 20 grains (0.3–1.3 gm.) or more, well diluted. It has the same therapeutic value as the potassium salt, but it is sometimes better borne by the stomach. Some clinicians prefer it to potassium

iodid, believing that the sodium ion is less depressing than the potassium ion, but it has been shown that the administration of potassium iodid does not produce a corresponding rise in the potassium content of the blood, but a definite rise of the sodium content, the exchange of ions apparently occurring during the process of absorption.

AMMONII IODIDUM, U. S. P.

(Ammonium Iodid, NH_4I)

Ammonium iodid occurs in minute colorless, cubical crystals or white granular powder, of sharp, saline taste. On exposure to air it attracts moisture, and becomes yellowish-brown from the loss of ammonia and the liberation of iodine. It is soluble in 0.6 part of water or in 3.7 parts of alcohol. The dose is from 3 to 15 grains (0.2–1.0 gm.), or more, in dilute solution. Excepting that it is somewhat more irritating to the stomach, it has the same properties as potassium iodid.

STRONTII IODIDUM, U. S. P.

(Strontium Iodid, $\text{SrI}_2 + 6\text{H}_2\text{O}$)

Strontium iodid occurs as colorless hexagonal plates or as a white granular powder, deliquescent, and of a bitterish, saline taste. It is soluble in 0.2 part of water. The dose is from 5 to 20 grains (0.3–1.3 gm.), or more, in dilute solution.

Strontium iodid has no special advantages over potassium or sodium iodid.

ACIDUM HYDRIODICUM

(Hydriodic Acid, HI)

Hydriodic acid is official as diluted hydriodic acid (*Acidum Hydriodicum Dilutum*, U. S. P.), which contains 10 per cent. by weight of the absolute acid, and as the syrup of hydriodic acid (*Syrupus Acidi Hydriodici*, U. S. P.), which contains 1 per cent. by weight of the absolute acid. The action of these preparations is feeble, but resembles that of the iodids. The dose of the diluted acid is from 5 to 10 minims (0.3–0.6 mil), and of the syrup $\frac{1}{2}$ to 2 fluidrams (2.0–8.0 mils).

IODUM, U. S. P.

(Iodine, I)

Iodine is a non-metallic element found largely in seaweed. It occurs in heavy, bluish-black, friable crystals, having a metallic luster, a peculiar odor, and a sharp, acrid taste. On heating

it emits a violet-colored vapor. It dissolves in 2950 parts of water, in 12.5 parts of alcohol, and is freely soluble in ether, chloroform, or solutions of potassium iodid.

PREPARATIONS	DOSE
Tinctura Iodi, U. S. P. (7 per cent.).....	1-5 min. (0.06-0.3 mil)
Liquor Iodi Compositus, U. S. P. (Lugol's solution: 5 per cent. of iodine in a 10 per cent. solution of potassium iodid).....	1-10 min. (0.06-0.6 mil)
Unguentum Iodi, U. S. P. (4 per cent. of iodine and 4 per cent. of potassium iodid).	

Pharmacologic Action.—When applied to the skin, iodine stains it a yellowish-brown color and causes burning and itching. Strong solutions produce vesication. Mucous membranes are especially sensitive to its irritant action. Injections beneath the skin or into serous sacs excite intense pain and severe inflammatory reaction. Iodine, in the form of the tincture, is an energetic germicide, being especially destructive to staphylococcus albus and other organisms of the skin.

When taken internally, iodine is rapidly absorbed in the form of iodides and soon reappears in all the secretions of the body. The bulk of it is eliminated in the urine, also in the form of iodides. In medicinal doses the drug exerts the same influence as potassium iodide, and if given continuously, induces all the phenomena of *iodism* (p. 326). Single large doses produce gastro-enteritis, respiratory failure, and collapse. Anuria and albuminuria have also been observed. Cases of fatal poisoning have been reported from its injection into large cysts and also from its too free use externally.

The *treatment of acute iodine-poisoning* consists in evacuating the stomach, administering starch or starchy foods (flour, arrow-root) as antidotes, and maintaining the respiration and circulation by hypodermic injections of alcohol, strychnine, digitalis, etc.

Therapeutics.—Iodine is a valuable *disinfectant* for use on the skin before operations and for wound treatment. Either a simple 5 or 10 per cent. alcoholic solution or the official tincture, which contains also potassium iodide, may be used for the purpose. For the skin a simple alcoholic solution is probably preferable. The tincture of iodine is a useful counterirritant in conditions requiring a mild but persistent effect, such as *pleurisy*, *bronchitis*, *laryngitis*, *synovitis*, *arthritis*, *neuritis*, *myalgia*, and similar inflammatory affections. It is best applied by means of a camel's-hair brush, one or two coats being painted over the part at intervals of a day or two. For children it should be diluted with 2 or 3 parts of alcohol. If the application proves too painful, the iodine should be removed with dilute alcohol, or, better, with

a solution of potassium iodid, and the part dressed with starch jelly. Stains may be removed by a warm concentrated solution of sodium thiosulphate (hyposulphite).

Preparations of iodin are sometimes efficacious in bringing about resolution in various forms of *adenitis*, provided they are applied early and before suppuration has commenced. A broad ring may be painted with the tincture around the swelling, or the ointment may be thoroughly, but gently, rubbed into it. *Ganglion*, *hydrocele*, and *spinal meningocele* are sometimes successfully treated by evacuating the fluid and then injecting tincture of iodin into the sac. Iodin has also been used, both internally and externally, with some success in the treatment of *simple goiter*. Local applications of Lugol's solution have long been held in high repute in certain chronic catarrhal processes attended by glandular hypertrophy, such as *rhinitis*, *pharyngitis* and *endometritis*. In *chilblain* an application of tincture of iodin and glycerin sometimes acts very favorably.

Incompatibles.—Alkaloids, mineral salts, ammonia, carbonates, starch, and mucilage of acacia. Iodin acts violently with oil of turpentine and many other volatile oils. Tincture of iodin is also incompatible with aqueous preparations. In the so-called "colorless solutions of iodin" the iodin is replaced by iodids.

Organic Iodin Preparations.—Various attempts have been made to lessen the irritant effects of iodin on the stomach and to prolong its retention in the body by combining the drug with fat or albumin. The preparation known as *iodipin* represents, perhaps, the most successful of these attempts. It is an addition-product of iodin (10 per cent. or 25 per cent.) and oil of sesame, which, according to Winternitz, is not decomposed in the stomach, but in the intestine. The 10 per cent. preparation is administered by the mouth in doses of $\frac{1}{2}$ to 2 drams (2.0–8.0 mls). It is generally well borne, but its oily taste frequently proves objectionable. The 25 per cent. iodipin is used for subcutaneous injection, about $\frac{1}{2}$ to 1 dram (2.0–4.0 mls), slightly warmed, being injected daily between the skin and muscle of the gluteal region.

Sajodin is an iodized fat with properties similar to those of iodipin. *Iodoalbin* and *Iodo-casein* are somewhat unstable iodized albumins.

AURI ET SODII CHLORIDUM, U. S. P.

(Gold and Sodium Chlorid, $\text{AuCl}_3 + \text{NaCl}$)

The gold and sodium chlorid of the Pharmacopœia is a mixture of equal parts, by weight, of anhydrous gold chlorid and

sodium chlorid. It is an orange-yellow powder, slightly deliquescent, of a saline and metallic taste. It is freely soluble in water. The dose is from $\frac{1}{20}$ to $\frac{1}{8}$ grain (0.003–0.008 gm.), in pill.

Pharmacologic Action and Therapeutics.—Gold and sodium chlorid is supposed to act as an alterative and a tonic. Large doses have an irritant action and excite gastro-enteritis. It has been recommended in a number of diseases, especially in *diabetes, hysteria, neurasthenia, tertiary syphilis, chronic alcoholism, and sclerosis of the spinal cord*, but it is of very doubtful value.

COLCHICUM

(Meadow Saffron)

Colchicum is the corm and seed of *Colchicum autumnale*, a bulbous perennial growing in Southern Europe and Northern Africa. The corm is official as *Colchici cormus*, and the seed as *Colchici semen*. The active principle of the drug is the alkaloid, *colchicin* (*Colchicina*, U. S. P.), which is a pale yellow, amorphous or crystalline powder, odorless and of a bitter taste. It is soluble in 22 parts of water and freely soluble in alcohol. The dose of colchicin is from $\frac{1}{150}$ to $\frac{1}{50}$ grain (0.0004–0.0013 gm.).

PREPARATIONS

DOSE

Extractum Colchici Cormi, U. S. P.....	$\frac{1}{2}$ –2 gr. (0.03–0.13 gm.)
Fluidextractum Colchici Seminis, U. S. P.....	2–5 min. (0.1–0.3 mil)
Tinctura Colchici Seminis, U. S. P.....	10–30 min. (0.6–2.0 mils)
Vinum Colchici Seminis.....	10–30 min. (0.6 2.0 mils).

Pharmacologic Action.—In warm-blooded animals large doses of colchicum or of its alkaloid excite severe abdominal pains, nausea, vomiting, and diarrhea. The discharges are at first serous, but later they may become mucous and even bloody. These symptoms are followed by progressive motor paralysis, enfeeblement of the circulation, collapse, and finally by death from asphyxia.

Postmortem examination usually reveals pronounced inflammatory lesions in the alimentary canal. Fatal poisoning has occurred from the ingestion of less than 3 drams (11.0 mils) of the wine of the root (U. S. P. 1890), and of less than $\frac{1}{2}$ grain (0.03 gm.) of colchicin.

The gastrointestinal features of the poisoning are probably due to the direct irritant action of the drug, although Jacobi attributes them to increased irritability of the motor nerves of the bowel, in consequence of which the muscular coat responds too vigorously to the ordinary stimuli. The paralysis, according

to Rossbach, results from depression of the central nervous system. Upon the circulation colchicum appears to have no direct influence. Both the water and the solids of the urine are somewhat increased after moderate doses of the drug, but large doses may be followed by suppression.

Treatment of Poisoning.—The stomach should be evacuated as speedily as possible. Albumin and other demulcents are useful in allaying irritation and in preventing further injury to the mucous membrane. Tannin is of no value as an antidote. Morphin may be given hypodermically to relieve pain and to inhibit peristalsis. The usual measures will be required to combat the collapse.

Therapeutics.—The only disease in which colchicum is of value is *gout*. The good and bad effects of the drug in chronic joint affections seem to have been known as early as the sixth century of the Christian era. For many years it was neglected by regular practitioners, although it still served as the basis of many celebrated nostrums. Later, the studies of Halford, Watson, and Garrod reestablished it in the confidence of the profession. The way in which gouty inflammation is affected by colchicum is not understood, and cannot be, until our knowledge of the pathology of the disease becomes more complete. The drug is most potent in acute gout, the pain and swelling of which it often relieves as if by magic; it is less efficacious in the chronic manifestations of the disease. In rheumatism it is useless.

Administration.—As colchicum is powerful for harm as well as for good, considerable care should be exercised in its administration. Only moderate doses should be employed, and these should be withdrawn or considerably reduced as soon as the pain has been relieved. Large doses, even if they do not excite irritation of the stomach or purging, may, by suppressing the local manifestations too abruptly, cause the grave visceral disturbances to which the term retrocedent gout has been applied. The tincture and the wine are reliable preparations; they should be taken, well diluted, after food. Alkalis are useful adjuvants, and may be combined with the colchicum, as in the following formula:

R̄. Potassii bicarbonatis..... ℥ij (8.0 gm.)
 Vini colchici seminis..... f ℥iiss (10.0 mls)
 Aquæ menthæ piperitæ.... q. s. ad f ℥iv (120.0 mls).—M.

SIG.—A tablespoonful in a wineglassful of water thrice daily, after meals.

Colchicin is a convenient form for administering the drug in pills or capsules.

GUAIACUM, U. S. P.

(Guaiac)

Guaiac is the resin of *Guaiacum officinale* (Lignum vitæ), a large tree growing in the West Indies and South America. It appears as irregular masses, of a reddish-brown color, turning greenish-brown on exposure, and has an aromatic odor and an acrid taste. It is soluble in alcohol and in alkaline fluids, but insoluble in water. Alcoholic solutions turn blue on the addition of oxidizing agents. It contains several resinous acids and aromatic oils and gums. The dose is from 5 to 30 grains (0.3–2.0 gm.).

PREPARATIONS

DOSE

Tinctura Guaiaci, U. S. P. (20 per cent. of the resin).....	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls)
Tinctura Guaiaci Ammoniata, U. S. P. (20 per cent. of the resin in aromatic spirit of ammonia).....	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls).

Therapeutics.—Guaiac possesses considerable power, although less than colchicum, in relieving *gouty inflammation*. It is especially efficacious in the subacute and chronic forms of the disease. In acute gout it may be substituted advantageously for colchicum as soon as the pain has subsided.

According to Garrod and Luff, it is also effective as a preventive of gouty attacks when given in doses of 5 grains (0.3 gm.), gradually increased to 10 grains (0.6 gm.), three times a day. It has also been recommended in *acute tonsillitis* and *sore throat* of the rheumatic type.

Administration.—The tinctures are reliable preparations, but as they have a very disagreeable taste, they should be given in the form of an emulsion. The resin itself may be given in capsules, in cachets or in an emulsion.

R. Guaiaci.....	3iiss (10.0 gm.)
Acaciæ.....	q. s.
Syrupi.....	f 5iv (15.0 mls)
Aquæ cinnamomi.....	q. s. ad f 3iv (120.0 mls).
Misce et fiat emulsum.	

Sig.—A dessertspoonful in water after meals.

Incompatibles.—Mineral acids and spirit of nitrous ether. Water is incompatible with the tinctures.

SARSAPARILLA, U. S. P.

Sarsaparilla is the root of *Smilax medica* and of other species of *Smilax*, large perennial climbers growing in swampy places

in tropical America. It contains a volatile oil, resin, and several saponins.

PREPARATIONS	DOSE
Fluidextractum Sarsaparillæ, U. S. P.	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mils)
Fluidextractum Sarsaparillæ Compositum, U. S. P. (sarsaparilla, 75 parts; glycyrrhiza, 12 parts; sassafras, 10 parts; mezereum, 3 parts; glycerin, 10 parts; diluted alcohol to make 100 parts).....	$\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mils)
Syrupus Sarsaparillæ Compositus, U. S. P. (fl. ext. sarsaparilla, 20 parts; fl. ext. gly- cyrrhiza, 1.5 parts; fl. ext. senna, 1.5 parts; sugar, 65 parts; oil of sassafras, oil of gaul- theria, and oil of anise, of each, 0.02 part; water to make 100 parts).....	1–4 fl. dr. (4.0–15.0 mils).

Therapeutics.—The action of sarsaparilla is very feeble. It has been used as an alterative in *sypilis* and *tuberculosis*, but it is without value. The compound syrup is chiefly useful as a vehicle to disguise the taste of unpalatable drugs, particularly potassium iodid.

JAMBUL (Java Plum)

Jambul is the root and seeds of *Eugenia jambolana*, a large tree growing in the East Indies. The active constituent of the drug has not been determined. The seeds are more powerful than the root, and may be given powdered in doses of from 5 to 20 grains (0.3–1.3 gm.), in capsules.

PREPARATION	DOSE
Fluidextractum Jambul.....	10–30 min. (0.6–2.0 mils).

Therapeutics.—Jambul has been used solely as a remedy in *diabetes mellitus*, for which it was originally recommended by Banatvala, of Madras. Binz found that it lessened the excretion of sugar in phloridzin diabetes, but Minkowski found it absolutely useless in experimental pancreatic diabetes. Von Noorden, in a study of 600 cases of diabetes, concludes that while jambul has no very marked action on the elimination of sugar, it is a good adjuvant to dietetic and hygienic procedures.

CALCIU SULPHIDUM CRUDUM, U. S. P.

(Crude Calcium Sulphide, Sulphurated Lime, Calx Sulphurata)

Sulphurated lime is a mixture containing about 55 per cent. of calcium monsulphid, together with calcium sulphate and varying proportions of carbon. It is a pale gray or yellowish powder, having a nauseous, alkaline taste and a faint odor of

hydrogen sulphid. It is slightly soluble in water and insoluble in alcohol. On exposure to air it is gradually decomposed. The dose is from $\frac{1}{4}$ to 1 grain (0.016–0.06 gm.), in pills, capsules or powders.

Therapeutics.—As was first pointed out by Ringer, sulphurated lime possesses some power of preventing and arresting suppuration. It has been found occasionally useful in *pustular acne* and *boils*. In *follicular tonsillitis* and in *quinsy*, doses of $\frac{1}{20}$ grain (0.003 gm.) every hour sometimes yield good results. It is better to give small doses at short intervals than large doses infrequently, since the latter are more prone to derange digestion and to cause disagreeable eructations of sulphureted hydrogen. As the drug deteriorates on keeping, only fresh preparations should be used.

As a local remedy, in the form of Vlemineckx's solution, it is often efficacious in *acne rosacea*.

R. Calcis..... ʒss (15.5 gm.)
 Sulphuris sublimati..... ʒj (31.1 gm.)
 Aquæ..... fʒx (296.0 mls.)

Coque ad fʒvj (177.5 mls), deinde filtra.

Sig.—Dilute with 10 parts of water and apply to the affected parts.

ICHTHYOL

(Ammonium Sulpho-ichthyolate)

Ichthyol is the ammonium salt of ichthyol sulphonic acid. The latter is the product of the action of sulphuric acid on an oily substance obtained by the destructive distillation of a bituminous mineral rich in fossil fish, found in the Tyrol. It is a thick, reddish-brown liquid, having a bituminous odor and taste. It is soluble in water and in a mixture of alcohol and ether, miscible with oils and glycerin in all proportions, and almost insoluble in strong alcohol or ether. It contains about 10 per cent. of sulphur, in the form of sulphids, sulfons and mercaptans, and to this ingredient its therapeutic properties, no doubt, are largely due. The dose is from 2 to 10 grains (0.13–0.65 gm.), in capsules or pills.

Pharmacologic Action.—When applied to the skin in concentrated form, ichthyol produces slight redness and burning. Its absorption through the unbroken skin is readily effected if gentle friction be used in the application. Besides being a local irritant, it is also an antiseptic. Taken internally, large doses cause eructations, nausea, vomiting and diarrhea.

Therapeutics.—Ichthyol is largely employed externally as an antiseptic and alterative. In the form of an ointment it

is useful in reducing *inflammatory swelling in glands and joints*. The best vehicle is lanolin, and the strength of the application may vary from 25 to 50 per cent. It is of some value as a local remedy in *erysipelas*, and in this disease it may be combined with blue ointment, as in the following formula, recommended by Roswell Park:

R̄.	Ichthyol.....	gr. xxx-xl (2.0-2.6 gm.)
	Resorcinolis.....	℥ss (2.0 gm.)
	Unguenti hydrargyri.....	℥iv (15.5 gm.)
	Adipis lanæ hydrosi.....	℥v (20.0 gm.).—M.

It is sometimes of service in *bruises, sprains, and chilblains*. Tampons saturated with ichthyol and glycerin (1 to 20 or 1 to 10) are often beneficial in *oöphoritis, perimetritis, endometritis, cervical catarrh*, and *gonorrhœal vaginitis*. In *atrophic rhinitis* ichthyol is sometimes useful in relieving the disagreeable symptoms. After the nares have been thoroughly cleansed, pledgets of cotton soaked in an aqueous solution (20 to 50 per cent.) should be inserted and allowed to remain for a period of from fifteen to twenty minutes, or in severe cases the drug may be applied pure by means of a probe armed with cotton.

The chief drawback to the use of ichthyol externally is its unpleasant, bituminous odor; this can be disguised in a measure by the addition of oil of bergamot (1:40).

Ichthyol has been used internally in a variety of diseases, particularly *tuberculosis* and *rheumatism*, but the testimony to its efficacy is not convincing.

Incompatibles.—Acids, alkalis, and alkaloidal salts.

Ichthalbin.—This preparation is a combination of ichthyol and albumin, appearing as a brownish powder, odorless, and nearly tasteless. The dose is from 5 to 10 grains (0.3-0.65 gm.). It has been thoroughly exploited as a substitute for ichthyol, both for internal and external use.

Ichthoform is a condensation product of ichthyol and formaldehyd. It has been recommended as a substitute for iodoform; but notwithstanding its freedom from odor it is less satisfactory than the older remedy.

Thiol.—This is a synthetic product obtained by the action of sulphur and sulphuric acid upon hydrocarbon as formed by the destructive distillation of peat. It was introduced as a substitute for ichthyol, but it has not proved a very formidable rival.

THYROIDEUM SICCUM, U. S. P.

(Desiccated Thyroid Glands, Thyroid Extract)

The profession is largely indebted to the observations of Kocher and to the experimental researches of Horsley for the

treatment of myxedema and allied conditions by the administration of thyroid gland. Kocher found that complete removal of the thyroid gland was followed in many instances by the appearance of a peculiar cachexia, the symptoms of which were almost identical with those of myxedema. Horsley showed that thyroidectomy in monkeys induced a similar condition. Schiff proved that the bad effects of thyroidectomy in animals could be averted by transplanting the gland in the peritoneum or subcutaneous tissue, and thereupon Horsley suggested this treatment for myxedematous conditions in man. Murray, in 1891, found that transplantation of the gland was unnecessary, as the same results could be secured from hypodermic injections of thyroid juice, and a little later Mackenzie demonstrated that thyroid feeding was equally efficacious.

In 1895 Baumann prepared a cleavage product from the gland, containing about 9 per cent. of iodine, which he named "iodothylin." Later, it was found that this product did not possess the therapeutic properties of the desiccated thyroid. In 1901 Oswald separated a protein, which he designated "thyroglobulin." This body possesses all the physiologic activity of the desiccated thyroid, but its iodine content is not much higher than that of the latter and it is not a single crystalline substance. In 1914 Kendall isolated a single chemical substance in pure crystalline form, which is apparently the active constituent of normal thyroid secretion. This body, which he has named *thyroxin*, is an amino-acid containing 65 per cent. of iodine. It has been produced synthetically by Osterberg. According to Plummer 150 grams of desiccated thyroid contain approximately 10 mg. of thyroxin.

Pharmacologic Action.—Large doses of thyroid extract produce a train of symptoms to which the term *thyroidism* has been applied. The most common manifestations of this intoxication are restlessness, insomnia, headache, palpitation of the heart, weakness of the circulation, anorexia, nausea, elevation of temperature, free perspiration, shortness of breath, tremors and twitchings of the limbs, prostration, and progressive loss of flesh. It will be observed that these symptoms are not unlike those of exophthalmic goiter, and to make the resemblance more complete, swelling of the thyroid gland and exophthalmos have occurred in a few instances. Standish has collected 11 cases of retrobulbar optic neuritis from the continued use of large doses.

In man, the most constant effect of thyroid extract in medicinal doses is increased metabolism, in consequence of which a considerable reduction in the body-weight occurs. Both the proteins and the fats suffer disintegration, but, according to

Vendelstadt, only one-sixth of the loss of weight can be attributed to the destruction of nitrogenous compounds, the rest being due to oxidation of fats and to increased excretion of water. The excessive destruction of proteins is made evident by the increased excretion in the urine of nitrogen and of phosphorus; the more rapid combustion of fats, by the increased elimination of carbon dioxid and the greater demand for oxygen.

In excess, thyroid extract frequently increases the rate of the pulse and lowers the arterial pressure. The manner in which these effects on the circulation are produced is not known. The hurried respiration observed in thyroidism may be due to the increased demand for oxygen. Even in moderate doses the drug usually increases the quantity of urine, and in large doses it may induce albuminuria and glycosuria.

The active constituent of thyroid extract must be decomposed in the body, at least to some extent, since after its administration iodine appears in the urine. Hutchinson found this element in the urine of a dog three hours after the administration of 15 grains (1 gm.) of colloid matter. That a part of the active constituent resists destruction in the body and escapes through avenues other than the kidneys is evidenced by the fact that an infant may acquire thyroidism through the mother's milk.

Therapeutics.—The diseases in which thyroid extract is most efficacious are *cretinism* and *myxedema of the adult*. In cretinism the results are often truly remarkable, especially when the treatment is instituted early. "Within six weeks," as Osler writes, "a poor, feeble-minded, toad-like caricature of humanity may be restored to mental and bodily health." In both affections the remedy must be continued throughout life, otherwise relapses occur. After the symptoms have been relieved, a weekly or biweekly dose may be all that is necessary to maintain normal metabolism. According to Plummer, a daily oral dose of 1.6 mg. of thyroxin will hold the basal metabolism of most thyroidless individuals within normal limits.

Thyroid extract is sometimes efficacious also in *infantilism*, *adiposis dolorosa* (Dercum's disease), *chlorosis*, and other diseases due to disturbance of the endocrine glands.

Thyroid extract sometimes proves efficacious, also, in *infantilism*, and in certain other conditions on the borderland of myxedema, in which imperfect mental and physical development is a prominent feature.

Considerable success has attended the use of the drug in *simple goiter*, especially in that form met with in adolescents. No effect, of course, should be expected from the treatment in

the old cystic goiters of adults. In exophthalmic goiter and toxic goiter thyroid feeding is harmful.

The loss of flesh following the administration of thyroid extract suggested its use in *obesity*. Ebstein believes that the treatment is not a rational one, since the drug causes a waste of the body-proteins as well as of the fats. The nitrogen loss may be controlled in a measure, however, by increasing the amount of protein in the food, so that it does not become an insurmountable objection to the treatment. In some cases of obesity the remedy proves entirely satisfactory and is not followed by any unpleasant consequences. It is most effective in the cases which bear a certain resemblance to myxedema, in which the skin is pale and the tissues are soft and flabby, and in cases of rapidly developing fatness at the time of the menopause. In certain skin diseases, particularly *psoriasis* and *ichthyosis*, thyroid is occasionally useful, but in the majority of cases it proves disappointing. According to Dercum, Mills, and others, small doses of the drug sometimes do good in *epilepsy*. It has been used empirically with asserted good results in *hemophilia*. It has been found efficacious in *nocturnal enuresis* in children who show evidences of defective growth and development.

Thyroid extract often acts beneficially in *amenorrhea*, the result of chlorosis or hypothyroidism, and Montgomery speaks favorably of it in *sterility* dependent upon obesity.

Administration.—Thyroid gland may be given in the form of the official preparation, *Thyroideum Siccum*, or of the active principle, *thyroxin*. Dried thyroid is the dried and pulverized glands of sheep and other animals used for food, one part representing approximately 5 parts of the fresh glands. It contains from 0.17 to 0.23 per cent. of iodine. The dose is from $\frac{1}{2}$ to 4 grains (0.03–0.25 gm.), in tablet or capsule form, from one to three times a day.

Thyroxin occurs as white crystalline needles, which are insoluble in water. The dose is from $\frac{1}{300}$ to $\frac{1}{32}$ grain (0.0002–0.002 gm.) by the mouth in the form of tablets, or intravenously in very weak alkaline solution (1 drop of a 10 per cent. solution of sodium hydroxid to a mil of water).

As persons vary considerably in their susceptibility to thyroid preparations, it is always advisable to begin with small doses and gradually to increase them. As a rule, it is better to give small doses frequently than large doses at long intervals. Exact dosage may be determined in any case by observing the effect of the treatment upon the basal metabolic rate. Treatment should be suspended, at least temporarily, on the very first appearance of untoward symptoms. Individuals with tubercu-

losis, chronic nephritis, and cardiac insufficiency are usually intolerant to thyroid medication.

HYPOPHYSIS CEREBRI

(Pituitary Body)

The differentiation in function between the two portions of the pituitary body cannot be made definitely at present, but the studies to date seem to show that the posterior portion furnishes a secretion that exercises a stimulating effect upon the involuntary muscles throughout the body, and that the anterior portion has a pronounced influence upon growth metabolism and sexual development. Hyperactivity of the hypophysis, presumably of the anterior lobe, if it occurs in early life, leads to marked overgrowth or gigantism, and if it occurs in later life, produces the condition known as acromegaly. On the other hand, decreased activity of the hypophysis leads to obesity, mental lethargy, sexual infantilism and increased tolerance to carbohydrates. The actions and uses of the extract of the posterior lobe have been considered under the heading Vasoconstrictors and Vasodilators (see p. 57). Extract of the anterior lobe, in doses of from 2 to 5 grains (0.13–0.3 gm.), three times a day, has been found useful in some cases of *dystrophia adiposogenitalis* (Fröhlich's syndrome) *pituitary infantilism* and *adiposis dolorosa* (Dercum's disease). In all of these conditions the effect of the pituitary substance is often increased by associating with it small doses of thyroid extract. Pituitary extract may act well also in *nocturnal enuresis*, *periodic headaches*, *recurring epileptoid* or *syncopal attacks*, when these occur in larval forms of hypopituitarism or dyspituitarism, shown by rapid growth, tardy sexual maturity, pubic hair of invert type, ready fatigability, low blood pressure and vasomotor disturbances.

SUPRARENALUM SICCUM

The chief function of the medullary tissue of the suprarenal glands appears to be the secretion of *epinephrin*, the actions and uses of which have been considered under the heading Vasomotor Constrictors and Vasomotor Dilators (see p. 57). The cortical tissue of the glands is apparently not concerned in the secretion of epinephrin. Most observers agree, however, that it furnishes some essential internal secretion and that the fatal result following extirpation of the suprarenal bodies is due to a loss of this secretion rather than a loss of epinephrin. The cortex seems also to have important relations to the activity of the sexual glands. It undergoes hypertrophy in pregnancy, and neoplasms involving

it (adrenal hypernephromas), occurring in young persons, are frequently associated with precocious development of the sexual organs. Both epinephrin and the official dried gland have sometimes been found temporarily beneficial in Addison's disease. Of 120 cases collected by Adams benefit resulted from this treatment in 25. As a rule, the dried gland has been more efficacious than the alkaloid. The usual dose is from 10 to 15 grains (0.6–1.0 gm.) a day, but in some cases three or four times this amount may be given with advantage. In certain polyglandular disturbances with *hypoadenia* as a prominent feature suprarenal extract may also be of service. Thus, Cushing observed marked benefit from the drug in the case of a eunuchoid giant with asthenia, pigmentation and low bloodpressure.

PARATHYROIDEUM SICCUM

It has been suggested that the parathyroids have some influence upon calcium metabolism, as removal of these glands results in severe nervous disturbances, especially tetany, and the effects are offset, at least temporarily, by the administration of calcium salts. An extract of parathyroid glands has been used in *tetany* occurring spontaneously, but without much success. The drug has also been used to some extent in *paralysis agitans*, *chorea of adults*, and *eclampsia*, but the results, on the whole, have been disappointing. The dose of the dried gland is $\frac{1}{10}$ grain (0.006 gm.) three or four times a day.

GLANDULA THYMUS

No definite statements can be made at present regarding the functions of the thymus gland. According to some investigators thymectomy in young animals retards the growth of the bony tissues and produces rachitic-like deformities. Other observations, however, indicate, on the contrary, that removal of the thymus is without effect or produces at most but transitory disturbances in health. According to Gudernatsch, the feeding of thymus extract to tadpoles stimulates their growth, but retards their metamorphosis to the frog-stage. It is possible that some sort of reciprocal relationship exists between the thymus, on the one hand, and the sexual glands and other organs of internal secretion, on the other. Extirpation of the thymus is said to hasten the development of the testes (Paton) and castration, to retard atrophy of the thymus (Henderson), and it is well established that Graves' disease is frequently associated with a persistent thymus.

Extract of thymus gland, in doses of from 5 to 15 grains (0.3–1.0 gm.), three times a day, has been used in a variety of diseases,

including *Graves disease*, *rickets*, *acromegaly*, *status lymphaticus*, *infantilism* and *adiposis dolorosa*, but the results have not been encouraging. Kinnicutt, in 1897, collected 62 cases of Graves' disease treated with the gland. Of these, 36 cases showed improvement; 25 were unimproved or showed aggravation of the symptoms. Of 20 cases treated by Mackenzie, 1 died, in 6 no improvement was observed, and in 13 there was some improvement. In none of the cases, however, was the effect so decided as to justify the conclusion that the thymus has any pronounced therapeutic activity.

TESTIS AND OVARIUM

In 1889 Brown-Séquard announced that he had personally experienced remarkable rejuvenating effects from injections of the extract of the testicles of rabbits. Emanating from such a high authority, this announcement led rapidly to the use of orchitic extracts, not only in senility, but in impotence, neurasthenia, hysteria, locomotor ataxia, and many other affections of the nervous system. More or less favorable results of this treatment have been reported, but in no instance has the good achieved been so decided as to convince a judicial observer that it was not due to mental suggestion rather than to the therapeutic effect of the drug itself. The important influence of the interstitial cells of the testicles in producing and maintaining the secondary sex characteristics has been well established. Castration in early childhood regularly causes impotence, a loss of sexual desire and a eunuchoid state. Lydston, Morris, and Lichtenstern have each reported encouraging results from the implantation of human testicle from a living or dead subject into the scrotum or rectus muscle in cases of testicular insufficiency arising from traumatic injury or mumps. Testicular extracts have been given also by the mouth in cases of *infantilism of the eunuchoid type* and of *dystrophia adiposogenitalis*, but no appreciable benefit has been reported from the treatment.

It has been demonstrated that the ovaries exert a pronounced influence upon the development of the secondary sex characters, their internal secretion promoting female characteristics and hindering the obtrusion of male characteristics. It is not definitely known, however, whether this endocrinic activity is associated with the interstitial cells of the glands, with the corpus luteum, or with both of these structures. As therapeutic agents, ovarian extract and corpus luteum extract (lutein) have been used extensively, and with some success, for the relief of the *functional amenorrhea* or *oligomenorrhea* in young women, and of the hot flushes and various psychoneurotic manifestations of the

artificial or natural menopause. Graves has found ovarian therapy of value also in *pruritus*, *furunculosis*, *kraurosis*, and other affections of the vulva in elderly women suffering from deficient circulation in the external genitalia. In all of these conditions an extract of the entire fresh ovary seems to be more effective than corpus luteum extract, although some clinicians favor the latter. The average dose of either preparation is 5 grains (0.3 gm.) in capsule, three times a day. Hirst has obtained good results in the *nausea* and *vomiting* of *pregnancy* from intramuscular injections of a soluble corpus luteum powder. One-third grain (0.02 gm.) of the drug in 15 minims (1.0 mil) of normal salt solution is injected daily or every other day, over a period of from one to two weeks.

ANTIPYRETICS OR FEBRIFUGES

The body derives its heat from the oxidation of fats, carbohydrates and proteins contained in foodstuffs and in the organized constituents of the tissues and loses it mainly by radiation and conduction from the skin, and the evaporation of water from the skin and lungs. Normally, heat-production and heat-dissipation are so evenly balanced that a mean temperature of 98.45° F. (36.9° C.) in the axilla is maintained, notwithstanding considerable variations in the outside temperature.

Antipyretics are drugs that lower temperature when it is abnormally high. They exert but little influence upon the normal temperature. Some of them, such as *acetanilid*, *acetphenetidin*, and *antipyrin*, act directly on the heat-regulating centers in such a way that the standard of temperature is brought to a lower level, where it is maintained for a limited period; some, such as *alcohol*, through their influence on the circulation, increase the dissipation of heat; while others, such as *quinin*, lessen the production of heat by diminishing the destruction of proteins.

Diaphoretics lower temperature by increasing the loss of heat due to the evaporation of sweat.

Cold applications increase the heat loss by conduction.

Indication.—Antipyretics are employed to lower temperature in febrile states. They are indicated, however, only when the temperature is sufficiently high as to be in itself a source of actual danger or of considerable discomfort to the patient. When used repeatedly at short intervals they are all more or less depressing. On the other hand, cold bathing has a stimulant as well as an antipyretic effect, and for this reason, when it can be carried out satisfactorily, it is always preferable to the use of drugs.

The most important antipyretics are:

Acetanilid	} benzol derivatives	Quinin
Acetphenetidin		
Antipyrin		Aconite.

Salicylic acid, *phenol*, and *guaiacol* also lower temperature in febrile states, but they are not used for this purpose.

ACETANILIDUM, U. S. P.

(Acetanilid, Antifebrin, $\text{C}_6\text{H}_5\text{NH}\cdot\text{CH}_3\text{CO}$)

Acetanilid is a derivative of anilin ($\text{C}_6\text{H}_5\cdot\text{NH}_2$), an atom of hydrogen in the latter being replaced by the acetyl radical. It is a colorless, shining, crystalline powder, odorless, and of a slightly burning taste. It is soluble in 190 parts of water, in 3.4 parts of alcohol, or in 17 parts of ether. The dose is from 3 to 10 grains (0.2–0.65 gm.).

Pharmacologic Action.—In health, a single moderate dose of acetanilid—7 grains—0.5 gm.—produces no appreciable effect. In fever, however, it induces a pronounced fall in temperature, which begins, as a rule, within two hours and lasts a variable time, usually three or four hours. The fall in temperature, which is almost always accompanied by free perspiration, is apparently due to dilatation of the cutaneous vessels and increased heat loss by radiation, an effect, which in turn, is the result of direct depression of the heat-regulating centers in the brain. Acetanilid does not lower the temperature after section of the spinal cord in the cervical region.

Circulation.—In ordinary doses acetanilid has usually no pronounced effect upon the circulation, but large doses, and occasionally even moderate therapeutic doses, powerfully depress the vasomotor system and produce collapse. Individuals vary considerably in their susceptibility to the collapse action of the drug. Generally speaking, febrile patients are more prone to circulatory failure than others, as the direct collapse effect of the antipyretic is augmented by the loss of the stimulating influence of the high temperature.

Blood.—After large doses of acetanilid the blood acquires a brownish color, owing to the formation of methemoglobin. The corpuscles themselves, however, do not undergo disintegration unless an excessive amount has been taken. Cyanosis develops as a result of the methemoglobinemia.

Respiration.—The drug seems to have no direct effect on respiration. In poisoning there is pronounced dyspnea, but this is probably due to the changes in the red blood-corpuscles and the circulatory depression.

Nervous System.—Our knowledge of the action of acetanilid on the central nervous system is very incomplete. The fact that the drug relieves headache and neuralgic pain and has a slight tendency to produce sleep, indicates, however, that it has a specific depressing effect upon the perceptive centers of the cerebrum. As large doses of acetanilid also lessen the tendency to epileptiform convulsions, choreic movements, etc., it is probable that the drug also depresses somewhat the motor centers of the brain. Unlike morphin, acetanilid in ordinary doses does not depress the intellectual powers. Locally, on mucous membranes and raw surfaces, the drug produces a slight analgesic effect by depressing the endings of the sensory nerves. Bokai and others assert that in frogs direct applications depress also the endings of the motor nerves.

Metabolism.—As the testimony concerning the action of acetanilid upon nitrogen and CO_2 excretion is highly contradictory, the conclusion may be drawn that the drug has no pronounced effects one way or the other upon tissue-metabolism.

Absorption and Excretion.—Acetanilid is absorbed and excreted with considerable rapidity. It is largely oxidized in the body to paramidophenol ($\text{C}_6\text{H}_4\text{OH.NH}_2$), which is apparently responsible for all of its antipyretic and analgesic actions. It is excreted as the sulphate and glycuronate of paramidophenol almost entirely by the kidneys. The urine, owing to the presence of certain decomposition products, acquires a dark hue.

Action on Lower Organisms.—Although it is somewhat effective in inhibiting the multiplication of bacteria, acetanilid is but a feeble germicide.

Toxicology.—Many deaths have resulted from the indiscriminate use of headache nostrums containing acetanilid. The chief symptoms of *acute poisoning* are nausea and vomiting, cyanosis, coma and collapse. The treatment consists in washing out the stomach with an alkaline solution, maintaining the body-temperature and combating collapse with such drugs as atropin, strychnin and digitalis.

Chronic acetanilid-poisoning is characterized by cyanosis, anemia, disturbances of digestion, headache, dyspnea on exertion, circulatory depression and extreme muscular weakness.

Untoward Effects.—Idiosyncrasies to acetanilid are not uncommon. Some persons are so susceptible to its action that cyanosis and collapse follow the administration of the drug even in small doses. Summers has reported an instance in which 4 grains, repeated in 30 minutes, caused cyanosis, partial loss of consciousness, and grave collapse in a healthy

patient, who had many times previously taken the drug in much larger doses without ill effects.

Fortunately, in the vast majority of such cases recovery follows under appropriate treatment. Papular and erythematous rashes are occasionally induced by acetanilid, but not so frequently as by antipyrin.

Therapeutics.—Moderate doses of acetanilid (5 gr.—0.3 gm.) are sometimes useful in controlling the temperature in such diseases as *typhoid fever*, *scarlet fever*, and *erysipelas*. Nothing, however, is to be gained from the use of antipyretic drugs in these diseases when the temperature is not above 103° F. or 103.5° F., and is not causing much inconvenience to the patient. They should be employed only when the temperature itself is exciting considerable discomfort or when it is so high as to exert a baleful influence upon the functions of the vital organs; even then, hydrotherapy, on account of its stimulant effects, is almost always preferable if it can be satisfactorily carried out and is not precluded by some special feature of the case.

Acetanilid and its congeners, judiciously employed, are of great value in relieving certain forms of pain, particularly *headache*, *neuralgia*, *migraine*, *myalgia*, the *pains of influenza*, and even the *nerve-storms of locomotor ataxia*, but they have little or no influence upon the pain of acute inflammation, of traumatic conditions or of morbid growths.

Externally, it has sometimes been substituted for iodoform in the treatment of *wounds*, *burns*, *ulcers*, and *chancroidal sores*. Its advantages are its inexpensiveness and freedom from odor. It must be employed with caution, as it may be absorbed in sufficient quantity to produce toxic symptoms. This use of the drug appears to be decidedly dangerous in young children, no less than 30 cases of poisoning from it in infants having been reported.

Administration.—It may be administered in powders, capsules, tablets, or pills. When a prompt effect is desired, it should be given in solution, alcohol being used as a solvent before the diluent is added.

Incompatibles.—With alkaline bromids and iodids in aqueous solution it forms insoluble compounds. When triturated with antipyrin, chloral, thymol, or resorcin, it forms a semiliquid mass. When added to spirit of nitrous ether, the solution after a time turns yellow and then red.

Exalgin or methyl-acetanilid is also a derivative of anilin. It has no advantages over acetanilid, which it resembles very closely in its action. It has been used more as an analgesic than as an antipyretic. The dose is from 3 to 10 grains (0.2–0.6 gm.).

ACETPHENETIDINUM, U. S. P.

(Acetphenetidin, Phenacetin, $C_6H_4(OC_2H_5).NH.CH_3CO$)

Acetphenetidin, or phenacetin, is obtained from paramidophenol ($C_6H_4OH.NH_2$) by substituting for one H atom ethyl (C_2H_5) and for another H atom acetyl (C_2H_3O). Paramidophenol is anilin ($C_6H_5.NH_2$) with an H atom replaced by OH. Acetphenetidin occurs in white crystalline scales or as a fine crystalline powder, odorless, and of a slightly bitter taste. It is soluble in 15 parts of alcohol, but it is only sparingly soluble in water. The dose is from 5 to 10 grains (0.3–0.65 gm.).

Pharmacologic Action and Therapeutics.—Acetphenetidin has actions similar to those of acetanilid and antipyrin, although it is somewhat less toxic than either of these drugs. On the whole, it is the most satisfactory of the “coal-tar” antipyretics, and when used in moderate doses it is less likely to cause cyanosis, collapse, or cutaneous eruptions. It is excreted in the urine mainly as paramidophenol in combination with sulphuric and glycuronic acids.

Acetphenetidin may be substituted with advantage for acetanilid and antipyrin when an analgesic or antipyretic of the benzol group is indicated. In certain painful conditions, such as *myalgia* or *neuritis*, it may be combined, if necessary, with other analgesics, especially codein and the salicylic compounds, as in the following formula:

R̄. Acetphenetidini ʒi (4.0 gm.)
 Codeinæ sulphatis gr. ii (0.13 gm.)
 Acidi acetylsalicylici ʒi (4.0 gm.)—M.

Fiant chartulæ No. xii.

Sig.—One powder every 3 or 4 hours.

Lactophenin.—This compound is closely allied to acetphenetidin in that it is para-phenetidin with an atom of hydrogen replaced by the lactic acid radical lactyl, instead of by the acetic acid radical, acetyl. In addition to being an antipyretic and analgesic it has some power as a somnifacient. The dose is from 5 to 10 grains (0.3–0.6 gm.).

Phenocoll Hydrochlorid.—This phenetidin derivative represents an attempt to produce a soluble phenacetin. Chemically, it is glycocoll para-phenetidin hydrochlorid. It is a white, crystalline powder, soluble in about 16 parts of water. It is readily decomposed by alkalis and alkaline carbonates. The dose is from 5 to 10 grains (0.3–0.6 gm.). As an antipyretic and analgesic it appears to be a safe and an effective substitute for acetanilid and antipyrin. It has been used also in *rheumatism* and in *malarial fever*, but with very indifferent success.

Apolysin, Citrophen, and Kryofin.—These compounds, all phenetidin derivatives, have been introduced as rivals of acetphenetidin. Apolysin differs from acetphenetidin in containing a citric acid radical instead of an acetic acid radical. Citrophen differs from apolysin in containing 3 phenetidin groups instead of 1 to the molecule of citric acid. Kryofin differs from acetphenetidin in containing a methyl-glycollic acid radical instead of an acetic acid radical. The dose of any one of these compounds is from 5 to 10 grains (0.3–0.6 gm.).

ANTIPYRINA, U. S. P.

(Antipyrin, Phenazon, Phenyl-dimethyl-pyrazolon, $C_8H_9N_2O(CH_3)_2.C_6H_5$)

Antipyrin is a synthetic base obtained by acting on phenylhydrazin with diacetic ether, and then methylating the resulting monoethyl compound. Phenylhydrazin ($C_6H_5NH.NH_2$) is closely related in its chemical structure to anilin ($C_6H_5.NH_2$). Antipyrin occurs as a white, crystalline powder, odorless, and having a slightly bitter taste. It is soluble in less than 1 part of water and in 1.3 parts of alcohol.

Pharmacologic Action.—The actions of antipyrin are similar to those of acetanilid and acetphenetidin. However, the drug is slightly less toxic than acetanilid and a little more toxic than acetphenetidin, and it is somewhat more prone than either acetanilid or acetphenetidin to produce papular or erythematous skin eruptions. Upon mucous membranes, 10 to 20 per cent. solutions exert analgesic and vasoconstricting effects similar to those of cocain, but much less pronounced. Antipyrin is absorbed rapidly and excreted rapidly, most of it escaping undecomposed through the kidneys.

Therapeutics.—Antipyrin is employed internally for the same purposes as acetanilid and acetphenetidin. It has an advantage over both of these drugs in being freely soluble in water. As a depressomotor, it is sometimes of service in *epilepsy*, *whooping cough*, and *chorea*, but it must never be used over long periods. In epilepsy, if the attacks are very frequent, from 10 to 15 grains (0.6–1.0 gm.) a day may be given with bromids for a week or 10 days and then discontinued for 2 or 3 weeks before being resumed. The drug should be withdrawn at once, however, if cyanosis appears. In whooping cough it may be given alone or in combination with a bromid, as in the following formula:

℞. Antipyrinæ..... ʒi (4.0 gm.)
 Sodii bromidi..... ʒii (8.0 gm.)
 Glycerini..... f ʒii (8.0 mils)
 Aquæ menthæ piperitæ.... q. s. ad f ʒiv (120.0 mils).—M.

Sig.—Two teaspoonfuls in water every four hours for a child of six years.

Administration.—Antipyrin may be given by the mouth in the form of powders or capsules, but on account of its ready solubility it is perhaps best ordered in some aromatic water. In exceptional cases it may be administered by the rectum.

Incompatibles.—On account of its basic properties, antipyrin has a wide range of incompatibility. It is incompatible with iron salts, calomel, sodium bicarbonate, ammonia water, nitrites, phenol, and all preparations containing tannin. When triturated with hydrated chloral, alkaline salicylates, orthoform, or betanaphthol it forms a semi-liquid mass. When added to spirit of nitrous ether a green color results from the formation of isonitroso-antipyrin.

OTHER ANTIPYRETICS

Quinin (see p. 446).—In health the bodily temperature is not appreciably lowered by quinin unless the dose be excessive, but in febrile states the drug usually exerts a marked antipyretic influence when given in doses of from 20 to 30 grains (1.3–2.0 gm.). This effect on the temperature cannot be attributed to an action on the heat-regulating centers, since it occurs after section of the spinal cord; it appears to be due rather to a depression of nitrogen metabolism, in consequence of which there is a decrease in the production of heat.

The best results are obtained by giving the drug in one large dose a few hours before a natural remission is expected to occur. As a matter of fact, however, quinin is rarely used as an antipyretic at the present time. When it is deemed necessary to lower the temperature by means of drugs, the benzol derivatives, on account of the certainty and promptness of their action, the ease with which they may be administered, and their power to relieve headache and other pains incident to fever, are preferable to quinin, which lacks these advantages, and which, moreover, often disturbs the stomach.

Guaiacol (see p. 410).—In febrile diseases guaiacol, applied to the skin, acts as a prompt and powerful antipyretic. To secure the desired effect, about 30 minims (2.0 mls) should be slowly rubbed into the skin of the abdomen with a camel's-hair brush, and the part subsequently covered with a piece of waxed paper to prevent evaporation. The absorption of the drug, which usually occurs in a few minutes, is followed by a gradual fall of temperature, the lowest point being reached about three hours after the application. The reduction of temperature is associated with profuse perspiration, and is followed shortly by a rapid return of the fever, with marked chilliness. The

applications often cause marked depression, and for this reason guaiacol cannot be recommended as an antipyretic.

Aconite (see p. 52).—Compared with the benzol derivatives, aconite is but a feeble antipyretic. It lowers temperature probably by depressing the circulation. On account of its sedative influence on the circulation, it is a useful febrifuge in *acute inflammatory conditions* and in the *febrile diseases of childhood* when the pulse is rapid and strong. It is contraindicated in asthenic fevers. The best results are obtained by giving the tincture in small doses at frequent intervals. Spirit of nitrous ether and the solution of ammonium acetate are often used as synergists.

ASTRINGENTS

Astringents are substances which tend to shrink mucous membranes and denuded tissues by precipitating the proteins of the superficial cells. Applied in suitable concentration to inflamed surfaces, they form a protective coating against irritants of various kinds and by acting on the cells of superficial glands and capillaries they tend to lessen secretory activity and congestion.

Astringents are divided into two classes, *vegetable* and *mineral*. The former owe their activity to tannin.

There are but few astringents that are not also irritants, especially if employed in concentrated form. Some of the metallic salts are more irritant and caustic in their action than they are astringent. This is due in one instance to the irritant properties of the acid liberated by the union of the metal with the protein of the cells; in another instance to the intensely toxic nature of the metal itself; and in still another instance to the permeable texture of the coagulum that is formed by the first application of the salt.

Among the mineral astringents, the insoluble salts of bismuth and zinc have more of a sedative than an irritant action.

The chief *vegetable* astringents are:

Tannin	Gambir
Galls	Hæmatoxylon
Kino	Sumac
Krameria	Hamamelis.

The chief *mineral* astringents are:

Alum	Zinc oxid
Lead acetate	Zinc sulphate
Copper sulphate	Bismuth subnitrate
Silver nitrate	Bismuth subcarbonate

Calcium carbonate.

Iron salts (see p. 297) and weak solutions of mineral acids, especially sulphuric acid (see p. 491), also have an astringent action.

Indications.—Of the mild astringents, the insoluble salts of bismuth are useful as protectives in inflammatory conditions of the stomach and intestines, and zinc oxid as a protective in acute inflammatory conditions of the skin. The more active astringents, such as zinc sulphate and silver nitrate, are frequently employed in dilute solutions to lessen congestion and secretion in catarrhal inflammation of the eyes, throat, urethra, etc. Certain other astringents, particularly alum, ferric sulphate or chlorid, and tannin, are used locally to check small hemorrhages, their styptic properties depending upon their power to coagulate the albumin of the blood.

ACIDUM TANNICUM, U. S. P.

(Tannic Acid, Tannin, Gallotannic Acid, $\text{HC}_{14}\text{H}_9\text{O}_9$)

Tannin is the active constituent of all the vegetable astringents. It is derived from the nutgall, which contains from 30 to 60 per cent. of it. When pure it is a light-yellowish, amorphous powder, almost odorless, and of a strongly astringent taste. It is soluble in about 0.34 part of water, in 0.23 part of alcohol, or in 1 part of glycerin. The dose is from 3 to 10 grains (0.2–0.6 gm.).

PREPARATIONS

Glyceritum Acidi Tannici, U. S. P. (20 per cent.)

Unguentum Acidi Tannici, U. S. P. (20 per cent.)

Trochisci Acidi Tannici, U. S. P. (1 gr.—0.06 gm.—in each).

Pharmacologic Action.—When applied to mucous membranes or raw surfaces tannin precipitates the proteins of the superficial layer of cells and consequently produces an astringent effect. As it also coagulates blood, it serves as a styptic when it is brought in direct contact with injured capillaries or small veins. Its action in the stomach varies according to the absence or presence of food. In the empty stomach it is decidedly astringent. In the presence of food it loses much of its astringency by uniting with protein to form protein tannate, although a certain amount of tannin is liberated when the gastric contents become moderately acid. In the upper bowel, at least above the level at which the contents are decidedly alkaline, both the tannin that is set free from the protein tannate formed in the stomach and that which arrives from the stomach in the free state produce an astringent effect.

In moderate doses it disturbs digestion, interferes with absorp-

tion and causes constipation. In large doses it acts as an irritant and excites vomiting. In the intestine, tannin is converted into non-astringent alkaline gallates, small amounts of which are absorbed and later excreted by the kidneys.

Therapeutics.—Locally, tannin is used to check excessive secretion and to shrink relaxed mucous membranes. In *subacute and chronic laryngitis* and *pharyngitis* a solution of from 1 to 5 grains (0.06–0.3 gm.) to the ounce (30.0 mls) makes a useful spray. Some surgeons have found injections of the glycerite, more or less diluted, efficacious in *subacute and chronic urethritis*. The same preparation is frequently beneficial in *chronic vaginitis*, *leukorrhea*, *erosion of the uterine cervix*, and *chronic cervical endometritis*. Lotions and dusting-powders containing tannin sometimes act favorably in *hyperidrosis of the feet*.

When it can be brought in direct contact with a bleeding surface, tannin is a reliable hemostatic. In *epistaxis* strips of lint spread with vaselin and tannin acid make an efficient tampon. In *hematemesis* or *enterorrhagia* the drug may be given in full doses by the mouth. As it is absorbed in the form of alkaline gallates, which have no styptic power, it is valueless in bleeding remote from the point of absorption.

As it forms more or less insoluble tannates with *tartar emetic* and the *vegetable alkaloids*, it may be employed as a chemical antidote in *poisoning* by these drugs. Cantani and others have spoken highly of enteroclysis with a hot tannin solution (2 per cent.) in *Asiatic cholera*.

Administration.—If its action is desired in the stomach, tannin should be given in powder; if the intestine is to be reached, it should be given in pill.

Incompatibles.—Alkaloids, gelatin, lime-water, tartar emetic, and the salts of iron, silver, lead, and copper. When tannin is triturated with potassium chlorate the mixtue explodes with great violence; hence, when these two drugs are to be combined in solution, they should be dissolved separately before being brought together.

Tannalbin, Tannigen, and Tannoform.—Several attempts have been made to enhance the therapeutic value of tannin as an intestinal astringent by converting it into insoluble compounds that will pass through the stomach unchanged and will slowly liberate tannin in the intestines. The most important of these compounds are tannalbin, tannigen, and tannoform.

Tannalbin is a light-brown, odorless and tasteless powder, containing about 50 per cent. of tannin. It is prepared by subjecting tannin albuminate to dry heat for a considerable time. The dose for adults is from 15 to 20 grains (1.0–1.3 gm.),

in powders or cachets; for children, from 5 to 15 grains (0.3–1.0 gm.), in some mucilaginous vehicle or in powders.

Tannigen is an acetic ester of tannin, and appears as a yellowish, odorless, almost tasteless, hygroscopic powder, insoluble in water. As in the case of tannalbin, its astringent properties are not manifested until it reaches the bowel, where its decomposition is effected. It may be given in the same dose as tannalbin.

* Experience in the use of these two remedies warrants the opinion that they may be used interchangeably; that they are comparatively free from irritant properties, even when administered in large amounts; and that they have a definite, if but limited, field of usefulness in the treatment of *acute intestinal catarrh*. The chief indication for their employment is the continuation of profuse and watery discharges after the cause of the inflammation has been completely removed. In chronic diarrhea and in dysentery they usually prove disappointing, and in tuberculous enteritis, of course, no favorable results from them are to be expected.

Tannoform is a combination of tannin and formaldehyd. It appears as a pale-pink powder, insoluble in water. It escapes decomposition in the stomach, but in the intestine is slowly broken up, yielding free tannin and formaldehyd. The dose for an adult is from 3 to 5 grains (0.2–0.3 gm.); for a child, 1 to 3 grains (0.06–0.2 gm.). It has been recommended in *intestinal catarrh*, but it is too irritant for internal use. As an external remedy, however, it is not without value. A mixture of tannoform 1 part and Venetian talc 2 parts often acts favorably in *excessive sweating of the feet*.

ACIDUM GALLICUM, U. S. P.

(Gallic acid, $C_6H_2(OH)_3CO_2H + H_2O$)

Gallic acid is the hydrid of tannin, from which it is usually prepared by boiling with dilute sulphuric acid. It occurs in white or pale-fawn colored, silky needles, odorless, of an astringent or slightly acidulous taste, and permanent in the air. It is soluble in 87 parts of water, in 4.6 parts of alcohol, or in 10 parts of glycerin. It differs from tannic acid in not precipitating gelatin, albumin, or alkaloids. The dose is from 5 to 20 grains (0.3–1.3 gm.) in powders or capsules.

Pharmacologic Action and Therapeutics.—Locally, gallic acid is a very feeble astringent, but as it does not coagulate blood, it cannot be recommended as a styptic. When taken internally, it is absorbed as alkaline gallates and in this form it is

eventually excreted in the urine. It has an undeserved reputation as an astringent for checking hemorrhages from the lungs, kidneys, etc., for controlling night-sweats, and for diminishing the excessive secretion of urine in diabetes insipidus.

GALLA, U. S. P.

(Nutmeg, Gall)

Galls are excrescences produced by the stings and deposited ova of an insect in the bark or leaves of a plant. The official galls are caused by a species of *Cynips*, which deposits its eggs in the tender shoots of *Quercus infectoria*, an oak growing in the countries bordering on the Mediterranean. Their therapeutic activities depend upon tannic acid, of which they contain from 30 to 60 per cent.

PREPARATION

Unguentum Gallæ, U. S. P. (20 per cent.).

Therapeutics.—At the present time galls are not used internally. Nutmeg ointment with equal parts of stramonium ointment is a time honored remedy for *painful hemorrhoids*.

KINO, U. S. P., GAMBIR, U. S. P. AND KRAMERIA

Kino is the inspissated juice of *Pterocarpus Marsupium*, a large tree growing in the East Indies. The dose of the powdered drug is from 5 to 15 grains (0.3–1.0 gm.).

PREPARATION

DOSE

Tinctura Kino, U. S. P. $\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls).

Gambir is an extract from the leaves and twigs of *Ouroparia Gambir*, a climbing plant of the East Indies. It is identical with catechu of the British Pharmacopœia.

PREPARATION

DOSE

Tinctura Gambir Composita, U. S. P. (5 per cent., with 2.5 per cent. of Saigon cinnamon) $\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls).

Krameria, or rhatany, is the root of *Krameria triandra*, a low shrub growing on the mountains of Peru and Bolivia.

PREPARATIONS

DOSE

Tinctura Krameria. $\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls).

Therapeutics.—All these drugs contain large amounts of tannin, to which their astringent properties are due. They are sometimes employed to check excessive secretion in *acute diarrhea*. They should never be given, however, until the bowel

has been thoroughly cleared of irritant material. They are often prescribed with chalk and opium, as in the following formula:

R. Cretæ præparatæ.....	℥ij (8.0 gm.)
Tincturæ opii deodorati.....	℥xxx (1.3 mls)
Tincturæ kino.....	f ℥ij (8.0 mls)
Acaciæ.....	q. s.
Aquæ cinnamomi.....	q. s. ad f ℥iij (90.0 mls).—M.

Sig.—A teaspoonful every two or three hours for a child of three years.

HÆMATOXYLON

(Hematoxylon, Logwood)

Hematoxylon is the heart-wood of *Hæmatoxylon campechianum*, a small tree growing in Central America and the West Indies. Its chief constituents are tannin and a crystalline coloring principle, *hematoxylin*.

PREPARATIONS

DOSE

Decoctum Hæmatoxyli.....	½–1 fl. oz. (15.0–30.0 mls)
Extractum Hæmatoxyli.....	5–30 gr. (0.3–2.0 gm.).

Therapeutics.—Logwood has been used chiefly as an astringent in the *diarrhea of young children*. It is less active than kino, krameria or gambir, but more agreeable on account of its sweetish taste. It has a disadvantage in staining the diapers a blood-red color. *Hematoxylin* is not used medicinally, but it is extensively used for its tinctorial properties in preparing tissues for microscopic study.

RHUS GLABRA

(Sumac)

Sumac is the fruit of *Rhus glabra*, a shrub growing in waste places in North America. It contains, in addition to tannin, several acid mallates.

PREPARATION

Fluidextractum Rhois Glabræ.

Therapeutics.—Sumac is never used internally, but the fluidextract, diluted with from 6 to 8 parts water, makes an efficient mouth-wash or gargle in *mercurial stomatitis* and in *acute pharyngitis*, especially if a small amount of potassium chlorate be added, as in the following formula:

R. Potassii chloratis.....	℥j (4.0 gm.)
Fluidextracti rhois glabræ.....	f ℥j (30.0 mls)
Aquæ.....	q. s. ad f ℥vii (250.0 mls).—M.

Sig.—Use as a gargle.

HAMAMELIS

(Witch-hazel)

Hamamelis was formerly official as the bark (*Hamamelidis Cortex*) and the dried leaves (*Hamamelidis Folia*) of *Hamamelis virginiana*, a shrub widely distributed throughout North America. It contains a volatile oil, a small amount of tannin, and a bitter principle.

PREPARATIONS

DOSE

Fluidextractum Hamamelidis Foliorum.....	½-1 fl. dr. (2.0-4.0 mls)
Aqua Hamamelidis.....	1-4 fl. dr. (4.0-15.0 mls).

Therapeutics.—Hamamelis water has a popular reputation as a topical remedy for *sprains*, *bruises*, and *small wounds*. As an enema or lotion, it makes a soothing application in *painful hemorrhoids*. Diluted with water, 1 part to 3, it is used with benefit as a spray in *acute coryza*.

ALUMEN, U. S. P.

(Alum, Potassium Alum or Ammonium Alum, $\text{AlK}(\text{SO}_4)_2 + 12\text{H}_2\text{O}$ or $\text{AlNH}_4(\text{SO}_4)_2 + 12\text{H}_2\text{O}$)

Alum is the sulphate of aluminum and potassium or the sulphate of aluminum and ammonium. These compounds are of equal value and occur as large, colorless crystals or as white powders, odorless, and of a sweetish and strongly astringent taste. They are readily soluble in water or glycerin and are insoluble in alcohol. The usual dose is from 5 to 10 grains (0.3-0.6 gm.), but as an emetic from 1 to 2 drams (4.0-8.0 gm.) may be given.

PREPARATION

Alumen Exsiccatum, U. S. P. (dried or burnt alum).

Pharmacologic Action.—When applied to the broken skin or to mucous membranes, alum acts as a powerful astringent, precipitating the proteins of the superficial cells, coagulating the fluids, and contracting the tissues. When used too freely or in the form of dried alum, it acts as an irritant. It forms a firm coagulum with blood, and thus tends to arrest hemorrhage. Taken internally in small doses, it has an astringent effect and causes constipation. Large doses usually excite vomiting, but if retained, they induce gastro-enteritis.

Therapeutics.—Alum may be used as a local styptic in arresting *hemorrhages from small wounds*. A solution of from ½ to 1 dram (2.0-4.0 gm.) to the pint (0.5 L.) is sometimes efficacious in *leukorrhea*. Sprays of a weak solution—5 to 10 grains

(0.3–0.6 gm.) to the ounce (30.0 mls)—are sometimes of service in *subacute and chronic pharyngitis* and *laryngitis*, especially when there is much mucous secretion. Its prolonged use in the mouth is contraindicated on account of its destructive action on the teeth. Lotions of alum and diluted alcohol are sometimes employed in *hyperidrosis*. Dried alum has been used as a mild caustic for destroying *superfluous granulations*.

Internally, alum is no longer in use as an astringent. It is, however, a safe but somewhat uncertain *emetic*, and may be given to children in doses of a teaspoonful of the powdered drug in syrup, repeated once or twice if vomiting does not follow.

Incompatibles.—Alkalis and their carbonates, lead acetate, mercury, iron salts, and tannin.

Alumini Chloridum.—Aluminum chlorid is a white amorphous powder, deliquescent, and readily soluble in water. A 25 per cent. aqueous solution, dabbed on the affected parts every other day and allowed to dry, has been found useful in *excessive sweating of the feet and axillary regions*.

PLUMBUM

(Lead, Pb)

Metallic lead is obtained from a native sulphid and is not official; the following preparations, however, are recognized by the United States Pharmacopœia: Acetate, subacetate, and oxid.

Pharmacologic Action.—Upon the skin the soluble salts of lead have little or no effect, but when applied to denuded surfaces or to mucous membranes they act as astringents, and form a delicate protective coagulum. Unless applied in concentrated form, they exert, with the exception of the nitrate, a sedative rather than a corrosive action.

Taken internally, single, moderate doses of lead acetate produce no effect outside of the alimentary canal. They leave a sweetish, metallic taste in the mouth, with a feeling of dryness, and, owing to their astringent effect, they tend to cause constipation. Most of the drug escapes absorption and is discharged in the stools in the form of a sulphid. In very large doses lead acetate acts as an irritant poison and excites pain in the stomach, nausea and vomiting, great thirst, diarrhea, or, more rarely, constipation, and collapse. Death is often preceded by coma and convulsions. The form in which lead is absorbed is not definitely known, but it is supposed to circulate as an albuminate. It is eliminated in the bile, intestinal secretions, saliva, and milk, and probably, also, in the sweat. Ordi-

narily, its excretion is effected slowly, so that its continuous absorption, even in small quantities, is likely to lead to an accumulation of the metal in the tissues. Absorption of lead occurs not only from the alimentary canal, but to some extent also from the lungs and the skin.

Treatment of Acute Lead-poisoning.—The stomach should be emptied by means of the stomach-pump, unless vomiting has rendered this procedure unnecessary. A soluble sulphate (Epsom or Glauber's salt) is a chemical antidote, forming with the lead an insoluble sulphate. It should be given in excess, so that a purgative effect may also be secured. The resulting gastro-enteritis should be treated by the application of warm fomentations to the abdomen and the administration of opium and demulcent drinks.

Chronic Lead-poisoning or Plumbism.—Chronic lead-poisoning is caused by the slow absorption of lead and the accumulation of the metal in the system. As long as excretion keeps pace with absorption symptoms do not develop. The poison may enter the body through the respiratory tract, through the gastrointestinal tract, or through the skin. Lead dust in the air is especially dangerous, although doubtless a part of the dust that is breathed into the nose and mouth is swallowed. Cutaneous absorption of non-water-soluble compounds of lead is relatively unimportant (Weyl, Legge, Oliver, Edsall). All forms of lead are not equally poisonous. Of the compounds used in industry, the suboxid, which forms on the surface of melted lead, red lead (Pb_4O_5), and the carbonate are probably the most dangerous.

Plumbism may result from the accidental introduction of lead into the system through drinking water, through canned goods (solder), through candies or cakes colored with lead pigments, or through hair dyes containing lead; it may be brought about by the too prolonged use of the salts of lead for medicinal purposes or through taking diachylon (lead plaster) as an abortifacient, but much more frequently it is induced in workmen who are exposed to the dust or fumes of lead or who handle the metal or paints containing it. Indeed, of all so-called industrial poisons lead is the most productive of ill health. An occupation involving the use of lead is dangerous in proportion to its dustiness. Among 150 or more trades that entail exposure to lead the best known are lead mining and smelting, working in white lead and lead colors, making type, pipe and other articles of lead, plumbing, printing, stereotyping, lithography, tinning, coach polishing (sandpapering dried paint), production of storage batteries and accumulators, and glazing pottery, bath-tubs, tiles, etc. Among

the less conspicuous lead-using industries may be mentioned zinc smelting, brass and nickel polishing, file making (old method), finishing cut-glass, working with tin-foil and aluminum-foil, diamond cutting, commercial illustration, manufacture of rubber goods, laying electric cables, and handling of lead-dyed artificial flowers, yarns and wall-paper.

Individual susceptibility varies considerably. The incidence of plumbism is proportionately greater among female workers than among male workers. Age is not without influence, the young being more readily affected than the old. Alcoholism, reduced vitality from any cause, and unhygienic habits increase the liability to poisoning. The quantity of lead required to produce poisoning is not definitely known. The lowest estimate is that of Brouardel, who places it at 1 mg. per day. The length of exposure necessary to the development of symptoms varies according to circumstances from a few days to many years.

SYMPTOMS.—The early symptoms are, as a rule, indefinite, but are significant when occurring in a person who has been exposed to lead. There may be pallor, general weakness, loss of flesh, trembling of the fingers, pains in the muscles and joints (usually described as rheumatic), anorexia, digestive disturbances, and constipation, or constipation alternating with diarrhea. The later and more characteristic manifestations are intestinal colic; a blue line on the gums, muscular paralysis, and basophilic degeneration of the red blood corpuscles.

Colic.—This is usually preceded by digestive derangements and accompanied by obstinate constipation. The pain, which is probably an effect of vagus stimulation, occurs in paroxysms lasting from a few seconds to an hour or more, and is commonly most intense about the umbilicus, although it may be diffuse. In severe attacks the abdominal wall is rigid and retracted, the bloodpressure is high, and not rarely the pulse is small and infrequent. Vomiting occurs in about one-half of the cases. The paroxysms often continue to appear over a period of several days. Relapses are common and occasionally occur even without any renewal of exposure. Care must be taken not to confuse lead colic with other abdominal pains, such as occur in appendicitis, peptic ulcer, cholelithiasis, renal calculus, and sometimes in *tabes dorsalis*, floating kidney, and aneurysm of the abdominal aorta.

Blue Line.—This consists in bluish or grayish-black line at the margins of the gums, especially about the incisor and canine teeth. It is due to the precipitation of lead sulphid, which compound is formed from the circulating lead through the action of hydrogen sulphid that is given off by decomposing particles

of food. It is fairly constant, and while it does necessarily imply lead-poisoning, it signifies absorption of the metal. If the teeth are well cared for and the gums are healthy the lead-line may be absent. Blackish deposits on the teeth themselves may be excluded by pushing a small piece of white paper between the edge of the gum and the teeth (Stewart). Similar lines are produced by silver, bismuth, copper and other metals.

Paralysis.—This is apparently due to degeneration of the peripheral nerves, especially of their terminal filaments, although changes have occasionally been observed in the nerve-cells of the anterior horns of the spinal cord (Déjérine-Klumpke, Spiller, Nissl, Stieglitz). The paralysis is almost always bilateral and in the large majority of cases is confined to the muscles which are supplied by the musculospiral nerve below the branch which goes to the supinator longus. It usually shows itself, therefore, in weakness of the extensors and in the characteristic “wrist-drop.” In severe cases the intrinsic muscles of the hands also become involved. Eventually, the affected muscles may undergo atrophy and yield the reactions of degeneration. A tremor is often observed in the hands and fingers, but pain is exceptional, objective sensory changes are slight or wholly wanting, and pronounced contractures are uncommon. The predisposition of the extensors of the arm is probably due to the greater use of these muscles (Stieglitz, Edinger, and Teleky). Much less frequently the muscles of the upper arms are affected, and occasionally the muscles of the legs (peroneal group and extensors of the toes), especially in children, become paralyzed. Still more rarely the ocular muscles, the laryngeal muscles, or the intercostal muscles are involved or the paralysis begins in the feet and spreads upward, as in Landry’s disease. Ordinary polyneuritis is very uncommon, but general sensory disturbances, especially paresthesias, are somewhat frequently observed. Painful cramps of the muscles, especially those of the calves, may also appear. Relapses often occur when patients return to their work and occasionally even without any renewal of exposure.

Basic Granulation of the Erythrocytes.—This sign is a valuable aid in the diagnosis of plumbism, although it is sometimes absent and it may occur in other anemias. The characteristic feature is the appearance of granules of varying size in many or a few of the red cells when these are stained with basic dyes. Accompanying the basic granulation there is usually some reduction in the number of red cells and the percentage of hemoglobin, but, as a rule, the pallor of the skin is out of proportion to the actual anemia. The pallor has been ascribed to vasoconstriction.

Cerebral symptoms (encephalopathy) in plumbism are relatively rare, but sometimes develop very suddenly in severe cases and in alcoholics. Intense headache, epileptiform convulsions, delirium and coma are the most common. Occasionally, the symptoms resemble those of paretic dementia. Postmortem examination of the brain in encephalopathy has shown in some instances slight thickening of the pia, edema, and scattered small hemorrhages. It is important not to confuse true encephalopathy with uremia. *Chronic nephritis* (cirrhosis of the kidneys) and *arteriosclerosis* are both common in lead workers. The urine in many cases shows not only a small amount of albumin and a few casts, but also traces of hematoporphyrin. Some relation seems to exist between plumbism and *gout*, the latter being relatively frequent in lead workers.

Amblyopia, without ophthalmoscopic changes or with evidences of optic neuritis, occasionally develops. In addition to causing a deposition of lead sulphid in the gums, the continued absorption of lead is believed to favor the occurrence of *caries of the teeth* and *gingivitis*. *Parotitis*, probably due to ascending infection from the mouth, has been described by a number of writers. Sailer and Speese found *gastric achylia* in 10 out of 12 subjects of saturnism. Lead has an unfavorable influence upon gestation and upon offspring. From 20 to 25 per cent. of the pregnancies occurring in the wives of men giving evidences of plumbism terminate in *miscarriages* (Verhaeghe, Harris), and a large proportion of the surviving children of males affected by lead die a short time after birth (Legge, Mott), or are deficient in vitality.

DIAGNOSIS.—This rests upon the history of exposure, the blue line, colic, bilateral wrist-drop without involvement of the supinator longus, pallor, basic degeneration of the erythrocytes, and the demonstration of lead in the urine. The absence of any of these signs is, of course, without significance if other characteristic features are present, and particularly if these are associated with a clear source of poisoning. The occurrence of increasing weakness, pallor and digestive disturbances without obvious cause in a laborer should always lead to a careful inquiry into the nature of his occupation.

PROGNOSIS.—In the absence of any pronounced organic changes in the bloodvessels or kidneys and of encephalopathy the outlook is favorable. Lead palsy usually disappears in from a few months to a year, but when it is of long duration and accompanied by marked atrophy the prognosis for complete recovery is not good. Cerebral symptoms are always of grave significance.

PROPHYLAXIS.—Much can be done to prevent plumbism in

lead-work establishments. The requisites are a thorough knowledge on the part of both employer and employe of the danger that working in lead entails, periodic medical inspection of workers, the collection of dust and fumes, as far as possible, at the source by proper exhaust systems, the substitution of vacuum cleaning for dry sweeping, thorough ventilation, the use of respirators by men engaged in dry processes, provision of ample bathing facilities, general personal cleanliness, change of outer clothing before leaving the works, the avoidance of food in any place where work is carried on, the free use of protein food before beginning work, prohibition of smoking and chewing during work, and complete exclusion of alcohol.

TREATMENT.—The indications are to prevent further absorption of the poison, to favor elimination, and to relieve the immediate symptoms. Removal from exposure to lead is imperative. Potassium iodid, in doses of 5 to 10 grains (0.3–0.6 gm.) thrice daily is believed to hasten elimination of the lead, although the manner of its action is not apparent. Sulphur baths are also recommended. These are prepared by mixing in a wooden tub 3 or 4 ounces (90.0–120.0 gm.) of potassium sulphuret with about 20 gallons (75.0 L.) of water. Constipation should be relieved by saline cathartics, preferably Epsom salts, or by oil enemas. Belladonna in full doses is a useful adjuvant, as the constipation is of the spastic type. Colic will require hot applications and hypodermic injections of morphin and atropin. Benzyl benzoate (5–20 minims—0.3–1.3 mls), every two hours, is helpful, but less effective as an antispasmodic than atropin. For the paralysis, massage, electricity and strychnin should be used.

PLUMBI ACETAS, U. S. P.

(Lead Acetate, Sugar of Lead, $\text{Pb}(\text{C}_2\text{H}_3\text{O}_2)_2 + 3\text{H}_2\text{O}$)

Lead acetate occurs in heavy, colorless, efflorescent, prismatic crystals or crystalline masses, having a sweetish, metallic taste, and a faintly acetous odor. It is soluble in 1.4 parts of water or in 38 parts of alcohol. The dose is from 1 to 4 grains (0.065–0.26 gm.) in pills.

Therapeutics.—Internally, pills of lead acetate and opium are sometimes useful in controlling *subacute* and *chronic diarrhea*. Solutions of from 1 to 5 grains (0.06–0.3 gm.) to the ounce (30.0 mls), employed as injections, are of service in the stationary stage of *gonorrhea*.

The well-known “lead-water and laudanum” is usually made of the subacetate of lead, but the acetate may be substituted with advantage, as in the following formula:

R. Plumbi acetatis..... ʒj (4.0 gm.)
 Tincturæ opii..... fʒj (30.0 mls)
 Aquæ..... q. s. ad fʒviii (250.0 mls).—M.

Although the ingredients in this combination are chemically incompatible and the opium is without local analgesic effect, the mixture makes a useful sedative application in *bruises, sprains, superficial inflammation, and erysipelas*.

Incompatibles.—Acids, alkalis, sulphates, carbonates, chlorids, and tannin.

PLUMBI SUBACETAS

(Lead Subacetate, $\text{Pb}_2\text{O}(\text{C}_2\text{H}_3\text{O}_2)_2$)

The subacetate of lead is so unstable that it is employed only in solution.

PREPARATIONS

Liquor Plumbi Subacetatis, U. S. P. (Goulard's extract: contains 25 per cent. of lead subacetate)

Liquor Plumbi Subacetatis Dilutus, U. S. P. (lead-water: contains 1 per cent. of lead subacetate).

Therapeutics.—The solution of the subacetate of lead, diluted with 4 to 6 parts of water, is employed as a sedative lotion in *acute eczema, rhus poisoning, and erysipelas*. The official diluted solution is too weak to be of much service, although it is often used in preparing "lead-water and laudanum" (2 parts of lead-water to 1 part of laudanum).

OLEATUM PLUMBI

(Oleate of Lead, $\text{Pb}_2\text{C}_{18}\text{H}_{33}\text{O}_2$)

Oleate of lead is official as lead-plaster (*Emplastrum Plumbi*), which is prepared by stirring together a hot solution of lead acetate and soap. Lead plaster makes a useful protective dressing for *superficial ulcers and bed-sores*. An ointment composed of equal parts of lead-plaster and of vaselin makes an efficacious application in *subacute eczema and hyperidrosis*. In the latter affection, after the parts have been cleaned and dried, the ointment should be applied on strips of muslin, and renewed twice daily for two or three weeks, instructions being given to avoid washing the feet in water during the progress of the treatment. Lead-plaster also enters into diachylon ointment (*Unguentum Diachylon*, U. S. P.) and into all of the official plasters.

PLUMBI OXIDUM, U. S. P.

(Lead Oxid, Litharge, PbO)

Lead oxid is a heavy, reddish-yellow powder, odorless and tasteless, and insoluble in ordinary menstrua.

It is rarely employed except in preparing the solution of lead subacetate (*Liquor Plumbi Subacetatis*, U. S. P.).

CUPRI SULPHAS, U. S. P.

(Copper Sulphate, Blue Vitriol, $\text{Cu SO}_4 + 5\text{H}_2\text{O}$)

Copper sulphate occurs as large, transparent, deep-blue crystals or as a blue, granular powder, odorless, and of a nauseous, metallic taste. It is soluble in 2.5 parts of water or in 500 parts of alcohol. The dose as an astringent is from $\frac{1}{4}$ to 1 grain (0.016–0.06 gm.); as an emetic, 5 to 10 grains (0.3–0.6 gm.).

Pharmacologic Action.—Upon mucous membranes and raw surfaces copper sulphate in dilute form acts as an astringent; in concentrated form it acts as a mild caustic. Taken internally in large doses, it causes emesis by its direct irritant action on the stomach.

Copper sulphate is not a powerful bactericide, but it is very effective against certain lower forms of plant life, mere traces being sufficient to keep water free from algæ and fungi. It has a low toxicity for animals.

Toxicology.—Acute copper-poisoning is characterized by severe abdominal pain, a metallic taste in the mouth, and violent vomiting and purging, the ejecta often being mucous and bloody. Death may be preceded by delirium, convulsions, and coma. The bluish or greenish color of the vomit may serve to distinguish it from poisoning by other irritants. After death the gastrointestinal tract is found to be intensely inflamed, and sometimes ulcerated. Unless death occurs very promptly, there may be found also fatty changes in the liver and kidneys.

Treatment.—The antidotes are potassium ferrocyanid, magnesia, sodium carbonate, and soap. Demulcents, such as milk and eggs, should be given freely. Opium will be required to relieve the pain.

Chronic copper-poisoning is of doubtful occurrence; it is said to occasion gastrointestinal disturbances, cachexia, a green line on the gums, and a greenish discoloration of the hair.

Therapeutics.—Copper sulphate is a prompt and powerful emetic, but it is most too irritant for ordinary use. When administered once without effect, it is best not to repeat the dose.

In *phosphorus-poisoning* it is useful not only as an emetic, but also as an antidote, since it forms on the phosphorus an insoluble coating of metallic copper.

In *indolent ulcers*, *ulcerative stomatitis*, *chronic granular conjunctivitis* (*trachoma*), light applications of the solid crystal are often very useful for their stimulant effects. In *gonorrhea*, after the acute symptoms have subsided, an injection containing 2 grains (0.13 gm.) to the ounce (30.0 mls), gradually increased in strength, is sometimes efficacious.

Internally, in pill form combined with opium, it is occasionally of service in *obstinate chronic diarrhea*. Good results have been reported from parenchymatous injections of copper sulphate in *actinomycosis*. According to the size of the infiltration, varying quantities of a 1 per cent. aqueous solution are injected at intervals of a few days, until the lesion becomes soft.

ZINCUM

(Zinc, Zn)

Metallic zinc is not official. The soluble salts of zinc, such as the acetate, sulphate and chlorid, have actions similar to those of copper. They are astringent and antiseptic, and in concentrated form decidedly irritant. The insoluble salts, such as the oxid and the carbonate, are only feebly astringent and antiseptic, but are valuable as sedatives and protectives in inflammatory and ulcerative conditions of the skin.

Chronic Zinc-poisoning.—Workmen in brass foundries and zinc smelters and others repeatedly exposed to the fumes of zinc not rarely suffer from a chronic intoxication, of which the most frequent manifestations are recurring chills ("spelter chills"), resembling those of malaria, gastrointestinal disturbances, bronchitis and albuminuria. Alcoholism and malnutrition from any cause are predisposing factors.

ZINCI SULPHAS, U. S. P.

(Zinc Sulphate, White Vitriol, $\text{ZnSO}_4 + 7\text{H}_2\text{O}$)

Zinc sulphate occurs as colorless, transparent, rhombic crystals or as a granular, crystalline powder, odorless, and of an astringent metallic taste. It is soluble in 0.6 part of water or in 2.5 parts of glycerin, and is insoluble in alcohol. The dose as an astringent is from $\frac{1}{2}$ to 3 grains (0.03–0.2 gm.); as an emetic, 10 to 30 grains (0.6–2.0 gm.).

Pharmacologic Action.—In weak solution zinc sulphate exerts an astringent effect; in concentrated solution, an irritant or caustic effect. Administered by the mouth, large doses (20

gr.—1.3 gm.) excite emesis through their action on the stomach. Toxic doses induce severe gastro-enteritis.

The **treatment of poisoning** consists in the free exhibition of alkalis or their carbonates, and of demulcents, such as eggs and milk.

Therapeutics.—A solution containing $\frac{1}{2}$ grain (0.03 gm.), gradually increased to 5 or 6 grains (0.3–0.4 gm.), to the ounce (30.0 mls) makes an excellent injection in *gonorrhea* after the subsidence of acute symptoms. Weak solutions are sometimes of service in *leukorrhea*.

R. Zinci sulphatis
Aluminis. āā ʒiiss (6.0 gm.)
Glycerini. fʒvj (180.0 mls).—M.

Sig.—Add a tablespoonful to a quart of hot water, and use as an injection.

A solution of from 1 to 2 grains (0.06–0.1 gm.) to the ounce (30.0 mls) is a favorite collyrium in the later stages of *simple conjunctivitis*.

Internally, zinc sulphate is used only as an emetic (see p. 185).

Incompatibles.—Alkalis and their carbonates, vegetable astringents, lead acetate, silver nitrate, and lime-water.

ZINCI ACETAS, U. S. P.

(Zinc Acetate, $\text{Zn}(\text{C}_2\text{H}_3\text{O}_2)_2 + 2\text{H}_2\text{O}$)

Zinc acetate occurs in thin, colorless, six-sided plates, of a pearly luster, an acetous odor, and an astringent, metallic taste. It is soluble in 2.3 parts of water or in 30 parts of alcohol. It is used as an astringent for the same purposes as zinc sulphate.

ZINCI CHLORIDUM, U. S. P.

(Zinc Chlorid, ZnCl_2)

Zinc chlorid occurs in white, granular powder or porcelain-like masses, or molded pencils, very deliquescent, odorless, and of a caustic metallic taste. It is freely soluble in water or in alcohol.

Therapeutics.—Zinc chlorid is the most caustic of the zinc salts. At present it is rarely employed except as an escharotic in removing *superficial epitheliomata*. Its action is rather slow, and is attended with severe pain. It is best applied in the form of a paste, which may be made by mixing 1 part of zinc chlorid and 3 parts of flour with a saturated solution of cocain hydrochlorid.

The solution of zinc chlorid has an unmerited reputation as a disinfectant.

ZINCI OXIDUM, U. S. P.

(Zinc Oxid, ZnO)

Zinc oxid is an amorphous white powder, free from odor and taste, and insoluble in water or in alcohol.

PREPARATION

Unguentum Zinci Oxidi, U. S. P. (20 per cent. of zinc oxid in benzoinated lard).

Therapeutics.—The ointment of zinc oxid is extensively used as a protective and slightly astringent dressing for *burns*, *acute ulcers*, and *acute inflammatory skin diseases*. Dusting-powders containing zinc oxid, starch, and Venetian talc, in various proportions, are very serviceable in *vesicular eczema* and in *erythema intertrigo*.

℞. Zinci oxidi
Talcī purificati..... āā ʒj (4.0 gm.)
Pulveris amyli..... ʒij (8.0 gm.).—M.

Internally, zinc oxid has been employed as an antispasmodic and an antihydrotic, but it is useless for either of these purposes.

ZINCI CARBONAS

(Zinc Carbonate, $2\text{ZnCO}_3 \cdot 3\text{Zn(OH)}_2$)

Zinc carbonate is official in the form of precipitated zinc carbonate (*Zinci Carbonas Præcipitatus*, U. S. P.), which is an impalpable white powder, of variable composition, odorless and tasteless, and insoluble in ordinary menstrua.

An impure precipitated carbonate of zinc, known as *calamin*, was formerly official (1860).

Therapeutics.—Zinc carbonate resembles zinc oxid in appearance and in therapeutic properties. It is chiefly employed as a sedative and protective application in acute inflammatory affections of the skin, such as *eczema*, *erythema intertrigo*, and *dermatitis venenata*. It is often combined with zinc oxid, as in the following formula:

℞. Zinci carbonatis præcipitati
Zinci oxidi..... āā ʒiiss (10.0 gm.)
Glycerini..... fʒj (4.0 mls)
Liquoris calcis..... fʒij (60.0 mls)
Aquæ rosæ..... q. s. ad fʒvj (180.0 mls).—M.

ZINCI STEARAS, U. S. P.

Zinc stearate is a fine, white, bulky powder, tasteless and having a faint, characteristic odor. It is insoluble in water or alcohol.

It is employed chiefly as a dusting powder in inflammatory conditions of the skin. The drug must be used with care in the nursery, as partial asphyxia may occur in infants from its accidental aspiration.

ARGENTUM

(Silver, Ag)

Two preparations of silver are official: Silver nitrate (*Argenti Nitras*) and silver oxid (*Argenti Oxidum*), and of these only the nitrate is of therapeutic importance.

ARGENTI NITRAS, U. S. P.

(Silver Nitrate, Lunar Caustic, AgNO_3)

Silver nitrate occurs in colorless, transparent, tabular, rhombic crystals, odorless, of a caustic metallic taste, and soluble in 0.4 part of water or in 30 parts of alcohol. It turns dark on exposure to light. The dose is from $\frac{1}{6}$ to $\frac{1}{2}$ grain (0.01–0.03 gm.).

PREPARATION

Argenti Nitras Fusus, U. S. P. (fused silver nitrate or lunar caustic; silver nitrate hardened by the addition of hydrochloric acid and moulded into cones or pencils).

Pharmacologic Action.—Locally, silver nitrate is antiseptic and, according to the concentration in which it is used, astringent or caustic. When applied undiluted to the skin, it acts as a superficial caustic, producing a white slough which subsequently turns black on exposure to light. Upon mucous membranes and raw surfaces it acts in dilute form as an irritant astringent by precipitating the proteins of the superficial layer of cells, and in concentrated form as a caustic, coating the part with a white pellicle of silver albuminate. Its corrosive action, however, does extend very deeply, owing to the impenetrable nature of the coagulum that is at once formed. Silver nitrate is an energetic germicide, solutions of 1 : 1000 destroying most bacteria within a few minutes.

When taken internally in medicinal doses, it exerts no other influence than that of an astringent and an antiseptic. Being so readily precipitated by chlorids, proteins, and hydrochloric acid, its astringent action is chiefly expended on the mucous membrane of the stomach. The bulk of it escapes absorption, but that a small percentage enters the circulation is evident from the fact that the prolonged use of the drug is followed by a deposit of silver in the skin and internal organs. Very little is

known concerning its elimination; it is supposed to be excreted slowly and imperfectly in the urine.

Toxicology.—In large doses silver nitrate acts as an irritant poison, producing intense abdominal pain, persistent vomiting and purging, and collapse. White or blackish patches may be present on the lips and mucous membrane of the mouth. Death is sometimes preceded by delirium, convulsions, and coma.

Treatment.—Common salt is the best antidote. It forms with the poison an insoluble and inert chlorid of silver. Demulcents should also be used freely.

Argyria.—The long-continued use of silver nitrate, either internally or locally, may result in the permanent deposition of dark silver particles, probably organic, in the various tissues of the body. This pigmentation, which is known as argyria, is not likely to result from the internal use of the drug unless the total amount ingested has exceeded 100 or 150 grains (6.5–10.0 gm.), although occasionally it has been produced by a much smaller aggregate dose. Clinically, argyria is manifested by a peculiar bluish-gray or bluish-black discoloration of the skin and mucous membranes. There is, as a rule, no impairment of the general health. The condition is incurable.

Therapeutics.—At the present time silver nitrate is chiefly used for its action on *inflamed mucous membranes* and *ulcerated surfaces*. In *chronic ulcers* a solution of from 10 to 40 grains to the ounce (0.6–2.6 gm. to 30.0 mls) or the solid stick may be employed as a stimulant application. Silver nitrate is perhaps the best caustic for removing *exuberant* or *superfluous granulations*. Its employment in *poisoned wounds*, especially in the punctured variety, and in those resulting from the bites of rabid animals, is to be condemned on account of its superficial action and the premature closure of the orifice.

In *simple conjunctivitis*, when the discharge has become mucopurulent, the membrane may be painted with a solution containing from 3 to 5 grains to the ounce (0.2–0.3 gm. to 30.0 mls). In *purulent ophthalmia* and *ophthalmia neonatorum* the conjunctiva, after being thoroughly cleansed, may be touched with a 10-grain solution (0.65 gm. to 30.0 mls). Credé's prophylactic treatment, which consists in the instillation of 2 drops of a 2 per cent. solution into the eyes of the new-born child when gonorrhea in the mother is suspected, has given excellent results. It must be remembered that the long-continued use of collyria containing silver nitrate may be followed by permanent discoloration of the conjunctiva.

Copious irrigation of the urethra with hot solutions of silver nitrate (1:10,000) has been found serviceable in both *acute* and

subacute gonorrhea. Good results are obtained in *chronic cystitis* by washing out the bladder first with distilled water and then with a solution of silver nitrate (1:8000).

Solutions varying in strength from 10 to 20 grains to the ounce (0.6–1.3 gm. to 30.0 mils) are extensively employed in the treatment of *chronic stomatitis*, *chronic pharyngitis*, and *chronic laryngitis*. Light touches of the solid stick act very favorably upon *mucous patches*.

In *chronic dysentery* benefit often follows the use of copious injections into the bowel of solutions of silver nitrate (10–30 grains to the pint—0.65–2.0 gm. to 0.5 L.). These injections should be given two or three times a week, the fluid being introduced very slowly through a tube passed well up into the bowel. At first the amount injected should not exceed 1 pint (0.5 L.), but later 2 or 3 pints (1.0–1.5 L.) may be employed with advantage. If the fluid is not expelled within a few minutes, a solution of sodium chlorid should be injected to precipitate the silver salt.

Internally, silver nitrate is employed chiefly for its local action on the gastro-intestinal tract. In *chronic gastric catarrh* and in *ulcer of the stomach* no remedy, with the exception of bismuth subnitrate or bismuth subcarbonate, is so generally useful. In refractory catarrh of the stomach, especially when there is supersecretion or marked hyperesthesia of the mucous membrane, douching the stomach once or twice a week, first with a solution of silver nitrate (1 : 5000 to 1 : 2000) and then with plain water, is a valuable method of treatment. About a pint (0.5 L.) of the solution should be introduced through the douche at each operation. Silver nitrate is also used in *acute* and *chronic enteritis*, but with less benefit than in inflammatory diseases of the stomach.

The treatment of *epilepsy*, *locomotor ataxia*, and *chorea* by the administration of the salts of silver is only of historic interest.

Administration.—In affections of the stomach silver nitrate should be given in pill form, half an hour before meals. Powdered opium or extract of hyoscyamus may be used as an excipient. The administration of silver should not be continued for a longer period than six or eight weeks without interrupting the treatment for a like period.

If treated promptly, silver stains may be removed by a 10 per cent. solution of potassium iodid.

Incompatibles.—Organic matter, bromids, chlorids, iodids, cyanids, sulphids, carbonates, phosphates, arsenites, and hydrochloric acid. With creosote it is explosive.

COLLOIDAL SILVER PREPARATIONS

Colloidal silver preparations are made by dissolving reduced (colloid) silver, silver oxid, or a protein-silver precipitate in an

excess of denatured protein, and drying *in vacuo*. They are mixtures of metallic silver, silver oxid and silver-protein compounds, in varying proportions, all in colloidal form, and are miscible with water, forming permanent black or brown suspensions of the extremely minute insoluble particles. Such suspensions, or so-called solutions, do not contain free silver ions and do not precipitate proteins or chlorids. They are non-astringent, mildly irritant or non-irritant, and less powerful as germicides than silver nitrate. Stains produced on linen by colloidal silver preparations may be removed by a 1:1000 mercuric chlorid solution.

The important colloidal preparations on the market have been grouped in New and Non-official Remedies as follows:

- (A) Protargin Strong, or Protargol Type.
- (B) Protargin Mild, or Argyrol Type.
- (C) Collargol Type.

Protargin Strong (Protargal, Protargentum-Squibb, Etc.). The compounds of this type contain from 7 to 8.5 per cent. of silver, but are distinctly irritant and have the strongest germicidal action. They are of service in purulent *conjunctivitis* (1 to 10 per cent.), in *gonorrheal urethritis* (0.25 to 2 per cent.) and *suppurative otitis media* (2 to 5 per cent.). If applied to the eye over too long a period they may cause persistent hyperemia and tumefaction of the conjunctiva.

A *prophylactic treatment of venereal diseases*, which is very effective if practised within an hour or two of exposure, consists in washing the parts thoroughly with soap and water, then injecting into the urethra a 2-per cent. solution of protargin strong, and, finally, rubbing into the glans a 30-per cent. calomel ointment for five minutes.

Suspensions of protargin strong are best prepared by sprinkling the powder on the surface of cold water, and allowing it to diffuse slowly without stirring.

Protargin Mild (Argyrol, Cargentos, Solargentum-Squibb, Etc.).—Preparations of this type contain from 19 to 30 per cent. of silver, are non-irritant and are but feebly germicidal. It has been suggested that they act chiefly as detergents and protectives, but this theory scarcely accounts for their well-recognized efficacy in gonorrheal infection.

Protargin mild compounds have been used extensively and with considerable success in *acute and chronic gonorrheal urethritis* (5 to 10 per cent.), in *purulent conjunctivitis* (5 to 25 per cent.), *chronic cystitis* (3 per cent., gradually increased), and *inflammatory conditions* of the *nose and throat* (5 to 50 per cent.). In the

eye it produces permanent staining (local argyria) more quickly than silver nitrate, and when used for long periods may cause a persistent hyperemic condition (de Schweinitz).

Colloidal Silver (Collargol, Argentum Colloidale, Argentum Credé, Etc.).—This preparation contains a much larger percentage (78) of silver and a smaller proportion (22) of proteinate than either protargin mild or protargin strong. The commercial preparations often contain also appreciable amounts of ionized silver. It has been used chiefly by intravenous injection and as an ointment. Intravenous injections (10 to 20 mls of a 2-per cent. filtered solution) produce a reaction characterized by chill, fever and leucocytosis, and which may be due rather to the foreign proteins than to the silver (Bottner). Intravenous injections have been recommended especially for *septicemia*, but the results have been disappointing. In the form of 15-per cent. ointment (Unguentum Credé), colloidal silver has been used with more or less success in various localized infections, such as *erysipelas*, *lymphadenitis*, *septic phlebitis*, and *gonorrheal arthritis*.

BISMUTHUM

(Bismuth, Bi)

The following preparations of bismuth are official: Bismuth subnitrate (*Bismuthi Subnitratis*, U. S. P.), bismuth subcarbonate (*Bismuthi Subcarbonas*, U. S. P.), bismuth subgallate (*Bismuthi Subgallas*, U. S. P.), bismuth betanaphthol (*Bismuthi Betanaphtholas*, U. S. P.), and bismuth and ammonium citrate (*Bismuthi et Ammonii Citras*, U. S. P.). As the bismuth preparations are useful mainly on account of their insolubility, bismuth and ammonium citrate, which is very soluble, is superfluous.

BISMUTHI SUBNITRAS, U. S. P.

(Bismuth Subnitrate, $\text{BiONO}_3 + \text{H}_2\text{O}$)

Bismuth subnitrate is a heavy, white powder of a somewhat varying composition, odorless, almost tasteless, and slightly hygroscopic. It is almost insoluble in water and is entirely insoluble in alcohol. With moistened blue litmus paper it shows an acid reaction. The dose is from 10 to 30 grains (0.6–2.0 gm.).

Pharmacologic Action.—When taken internally, even in large doses, the effects of bismuth subnitrate are confined to the alimentary canal, its action being that of a protective and a feeble astringent and antiseptic. The drug has no constipating effect, except in the presence of catarrhal diarrhea. Since traces of bismuth are found in the urine, there must be some absorption,

but the amount of the metal entering the blood under ordinary conditions is too small to exert any special influence. The characteristic black stools following the administration of the drug are due to its partial conversion into a sulphid in the intestine. On the unbroken skin bismuth subnitrate acts simply as a protective, but on raw surfaces a small amount of the drug is dissolved, so that it acts also as an astringent and antiseptic. Absorption takes place somewhat readily from denuded parts.

Toxicology.—Enormous doses of bismuth subnitrate (2 to 4 ounces—60.0–120.0 gm.), such as were formerly used in x-ray diagnosis, not infrequently produce alarming symptoms, which are due not to the bismuth itself, but to nitrites liberated in the intestinal tract through the reducing action of putrefactive bacteria. The chief features of this form of poisoning are dyspnea, cyanosis, and, finally, arrest of the respiration. True bismuth intoxication has only rarely followed the internal use of the drug, but it has frequently resulted from its local application to denuded surfaces, sinuses, etc. The chief symptoms of the metallic type of poisoning are stomatitis with salivation, a black or brownish discoloration of the tongue and buccal mucous membrane, dysphagia, colicky pains, diarrhea, and albuminuria. In fatal cases necropsy has revealed ulceration of the colon with large purplish-black areas of discoloration, cloudy swelling of the viscera, and tubular nephritis. With microchemical tests, bismuth may be demonstrated in the kidneys, liver, spleen and intestines. The stomatitis is probably due to the excretion of bismuth salts by the salivary glands (Dalché) and the colonic ulceration, to capillary emboli produced by the precipitating action of hydrogen sulphid on the bismuth salts circulating in the blood (Steinfeld and Meyer). According to Higgins, there were on record up to 1916 forty-three cases of poisoning, thirteen of them fatal, following the local application of bismuth to granulating surfaces.

Therapeutics.—No remedy is so generally useful in allaying *gastrointestinal irritation* from various causes as bismuth subnitrate or subcarbonate, its effects being mainly that of a protective, although its action as a mild antiseptic and, in the case of the subcarbonate, its antacid properties, may in some cases be also beneficial. Both of these basic salts are standard remedies in *acute* and *chronic gastritis* and in *peptic ulcer*. In the latter affection from 20 to 30 grains (1.3–2.0 gm.) stirred up in water, may be given on an empty stomach several times a day. When the gastric acidity is high the subcarbonate is preferable to the subnitrate. Even in *gastric carcinoma*, bismuth sometimes affords temporary relief. It is also of much service in *gastralgia*

the result of *hyperchlorhydria*. Vomiting arising from gastric irritation often yields to it.

In *acute enteritis*, after the intestine has been thoroughly emptied, it almost invariably checks the diarrhea. In this condition it binds the sulphids, acts as a protective to the irritated mucous membrane, as an astringent and as an antiseptic, and, probably, like other finely divided inert substances, serves to absorb or fix the bacteria. Even in *acute dysentery* it is sometimes efficacious. In many cases of acute enteritis it may be combined advantageously with morphin or codein and some other antiseptic, as in the following formula:

℞. Morphinæ sulphatis..... gr. i (0.06 gm.)
 Phenylis salicylatis..... gr. xvi (1.0 gm.)
 Bismuthi subnitratis..... ʒvi (24.0 gm.).—M.
 Fiant chartulæ No. xvi.
 Sig.—One every three or four hours.

Locally, bismuth subnitrate, alone or with starch, may be used as a dusting-powder in *intertrigo* and other *acute erythematous skin diseases*. In the *second stage* of *gonorrhea* injections of bismuth subnitrate, 15 grains (1.0 gm.) to the ounce (30.0 mls) of glycerin and water, sometimes have a favorable action. The bismuth paste injections, introduced by Beck, in 1906, have proved serviceable in various *sinuses*, such as those resulting from *empyema*, *psaos abscess*, *tuberculous joints*, etc., although the treatment has not rarely been followed by poisoning. Two formulas are used, the one for early and the other for late treatment. The first is prepared by adding 33 parts of bismuth subnitrate to 67 parts of boiling petrolatum, and the second by adding 30 parts of bismuth subnitrate to a boiling mixture of petrolatum (60 parts), paraffin (5 parts) and white wax (5 parts). After the sinus has been thoroughly dried, the paste, which has been cooled sufficiently not to burn the tissues, is introduced slowly, every crevice being filled at one injection. Finally, a pad is applied to the mouth of the sinus to prevent the escape of the paste until it has hardened. The injections are made not oftener than once a week. Upon the first evidence of poisoning warm olive oil should be introduced into the cavity, allowed to remain 12 to 24 hours, and then withdrawn with the paste. The treatment is not appropriate for large pus sacs nor for acute suppurating cavities.

Administration.—Insoluble salts of bismuth are usually prescribed in powders or in capsules. Very large doses, however, may be given conveniently in water, the mixture being well shaken before each administration. Alkaline bicarbonates and sodium hyposulphite are incompatible with such mixtures. In

affections of the stomach the drug should be taken half an hour before meals.

BISMUTHI SUBCARBONAS, U. S. P.

(Bismuth Subcarbonate, Bismuth Oxycarbonate, $(\text{Bi}_2\text{O}_2\text{CO}_3)_2 \cdot \text{H}_2\text{O}$)

Bismuth subcarbonate resembles bismuth subnitrate in its physical properties and its pharmacologic action. Unlike the latter, however, it is a gastric antacid, and, therefore, is to be preferred as a protective to the mucous membrane of the stomach in *hyperchlorhydria with pain* and in most cases of *peptic ulcer*. Although as an antacid it has only one-third of the neutralizing power of sodium bicarbonate, its action is more prolonged, the breaking down into bismuth oxychlorid being effected very slowly. In hyperchlorhydria it may be combined advantageously with other antacids, as in the following formula:

R. Magnesii oxidi..... ʒiiss (10.0 gm.)
 Bismuthi subcarbonatis..... ʒiii (12.0 gm.)
 Sodii bicarbonatis..... ʒii (8.0 gm.).—M.
 Fiant chartulæ No. xx.
 Sig.—One powder half an hour after meals.

BISMUTHI SUBGALLAS, U. S. P.

(Bismuth Subgallate, Dermatol, $\text{Bi}(\text{OH})_2\text{C}_7\text{H}_5\text{O}_6$)

Bismuth subgallate is a fine, yellowish-white powder, odorless and tasteless, permanent, and insoluble in ordinary solvents. It should yield not less than 52 per cent. of bismuth oxid. The dose is from 5 to 30 grains (0.3–2.0 gm.).

Therapeutics.—Bismuth subgallate has been employed somewhat extensively as a protective and an astringent application for *burns* and *moist eczema*. It does not appear, however, to have been less harmful than other bismuth compounds when used externally. Internally, it has been used instead of the subnitrate and subcarbonate in *catarrhal affections of the stomach and intestine*, but it has no advantages over the older preparations.

BISMUTHI SUBSALICYLAS, U. S. P.

(Bismuth Subsaliicylate, $\text{Bi}(\text{C}_7\text{H}_5\text{O}_3)_3\text{Bi}_2\text{O}_3$)

Bismuth subsaliicylate is a white amorphous or crystalline powder, odorless and tasteless, and insoluble in water. It is used chiefly as an intestinal antiseptic and astringent in *diarrhea*. The dose is from 5 to 20 grains (0.3–1.3 gm.).

CALCII CARBONAS

(Calcium Carbonate, Chalk, CaCO_3)

Chalk is official in two forms: Precipitated calcium carbonate (*Calcii Carbonas Præcipitatus*, U. S. P.) and prepared chalk (*Creta Præparata*, U. S. P.), the latter being a native form of calcium carbonate freed from most of its impurities. The dose of either preparation is from 10 to 30 grains (0.65–2.0 gm.) or more.

PREPARATIONS

DOSE

Pulvis Cretæ Compositus, U. S. P. (prepared chalk, 30; acacia, 20; sugar, 50).....	5–40 gr. (0.3–2.6 gm.)
Mistura Cretæ, U. S. P. (compound chalk powder, 20; cinnamon water, 40; water, q. s. 100).....	1–4 fl. dr. (4.0–15.0 mls).

Therapeutics.—Chalk is a mild astringent and antacid, free from irritant properties. It may be employed in *acute inflammatory diarrhea* in the same manner as bismuth subnitrate. It is an excellent antacid when acidity of the stomach is associated with relaxation of the bowels. It may be prescribed as an *antidote* in poisoning by a *mineral acid* or by *oxalic acid*.

Externally, it is used as a dusting-powder in *erythematous eczema* and *intertrigo*. It is particularly useful in the *chafing of the genitalia and buttocks* of young children from irritation by urine. It enters into the composition of most *tooth-powders*.

R. Calcii carbonatis præcipitati.....	℥iii (90.0 gm.)
Pulveris saponis.....	℥ii (8.0 gm.)
Pulveris sacchari	
Pulveris amyli..... āā	℥iii (12.0 gm.)
Olei gaultheriæ.....	℥xxx (2.0 mls).—M.
Sig.—Tooth-powder.	

CERII OXALAS, U. S. P.

(Cerium Oxalate, $\text{Ce}_2(\text{C}_2\text{O}_4)_3 + 9\text{H}_2\text{O}$)

Cerium oxalate is a white, odorless, and tasteless powder, insoluble in water or in alcohol. The dose is from 5 to 15 grains (0.3–1.0 gm.), preferably in the form of a dry powder. It is not absorbed from the digestive tract, and, unlike the soluble oxalates, it is non-toxic. It is sometimes useful as an *anti-emetic* when vomiting is caused by irritation of the stomach, its action being mechanical, and similar to that of bismuth subnitrate. It is useless in central vomiting, although at one time it was highly recommended against the vomiting of pregnancy.

HEMOSTATICS

Hemostatics are agents that arrest hemorrhage. They all act in accordance with methods pursued by nature in spontaneously closing a bleeding vessel. If an artery be divided, it shrinks within its sheath, the contiguous structures fall in upon the bleeding orifice, and if the hemorrhage be copious, the force of the circulation diminishes and the coagulability of the blood increases. The choice of a hemostatic will largely depend upon the site of the hemorrhage—that is, whether it is in an accessible or in an inaccessible region. Hemorrhage from a large vessel in an accessible region should always be controlled by *mechanical means*—that is by ligature, pressure, torsion, acupressure, or cauterization. Many parts formerly considered inaccessible are no longer so regarded, and to-day surgical aid is sometimes wisely invoked to arrest excessive bleeding from such organs as the stomach and bowel, and even the brain.

Small external hemorrhages, especially capillary oozing, are often satisfactorily controlled by the direct application of agents that contract the vessels or that coagulate the albumin of the blood. The most potent local vasoconstrictors are *cold*, in the form of ice, and *epinephrin*; and the most powerful styptics are *ferric sulphate*, *ferric chlorid*, *alum* and *tannin*.

Three classes of drugs have been recommended to control hemorrhage in organs that must be reached through the circulation. The first includes *tannin* and certain *mineral salts* which have been found useful as local styptics or astringents; the second, drugs which cause vasoconstriction by stimulating the arterial muscle or the nerve-endings in the muscle, such as *ergot*; and the third various agents which tend to increase the coagulability of the blood, such as *blood-serum*, *extracts of various tissue cells*, *calcium salts*, and *gelatin*.

Drugs of the first two classes are useless. There is no reason to believe that tannin, for instance, exerts any influence outside of the alimentary canal, since it enters the blood only in small quantities and in such a form (alkaline gallates) that it loses its styptic and astringent properties. As regards the mineral astringents, such as lead acetate, it is known that not one of them enters the circulation in sufficient quantity to exert any favorable influence upon hemorrhage in a region remote from the point of absorption. Owing to its power to contract the smooth muscle of the uterus, ergot is undoubtedly of value in controlling certain forms of metrorrhagia, but its use in other internal hemorrhages, such as hematuria and hemoptysis, is irrational. Even if it had power to cause vasoconstriction when given internally in ordinary

doses, it is unreasonable to suppose that its effects would be limited to the vessel concerned in the bleeding, and unless this is the case, it should tend to do harm rather than good, as a universal narrowing of the blood-paths and a consequent increase in the bloodpressure must favor the escape of blood and also hinder the formation of an occluding thrombus. The use of a drug that lowers the bloodpressure is more rational, and, indeed, *nitroglycerin* has been given with asserted good results in hemoptysis.

Agents that favor coagulation of the blood, especially blood-serum and the tissue extracts containing elements concerned in the clotting of normal blood, have been found useful in the hemorrhagic diseases, such as hemophilia and purpura, as well as in bleeding occurring in hepatic disease, aplastic anemias, and some of the infections.

Blood-serum.—Since Weil, in 1905, first reported favorably upon its use in hemophilia, blood-serum has been employed in a great variety of hemorrhagic conditions, frequently without success, but sometimes with remarkably favorable results. The chief coagulation-accelerating substance contained in blood-serum is apparently thrombin, which normally forms clot from fibrinogen. Normal human serum is to be preferred, as it contains no foreign protein, but if it is not available fresh horse-serum may be substituted, although in using the latter the possibility of anaphylactic reactions must be borne in mind. It has been shown that old serum, such as antidiphtheria serum, may retard rather than hasten the clotting of blood, as on standing, even for a few days, the thrombin of serum is converted into an inactive form and in consequence the proportion of antithrombin is increased. Serum may be given subcutaneously in doses of 20 to 40 mils or, preferably, intravenously in doses of 10 to 30 mils, once in twenty-four hours. It may also be used locally on compresses if the bleeding point is accessible.

Coagulose is a dried product from horse serum. It may be applied dry to bleeding surfaces, or the contents of an ampule, which represent 10 mils of fresh serum, may be dissolved in sterile water and injected subcutaneously.

Whole Blood.—Whole blood has an advantage over serum in that it contains all the elements concerned in clotting. Administered intravenously, it has proved valuable in controlling hemorrhages in *hemophilia* (prothrombin deficit), *hemorrhagic disease of the newborn* (prothrombin deficit), *aplastic anemia* (prothrombin and blood-platelet deficiency) and *purpura hemorrhagica* (blood-platelet deficiency). From 50 to 500 mils may be injected, care being taken that the donor's blood is compatible with that of the patient, as shown by preliminary agglutination

and hemolysis tests. Whole blood or defibrinated blood may also be used locally to control external bleeding.

Tissue Extracts.—Extracts of various tissues hasten the coagulation of blood because they are rich in thromboplastin, which is a lipoid, probably kephalin. According to Howell, prothrombin within the vessels is held in combination with antithrombin and intravascular clotting is thereby prevented. Thromboplastin neutralizes the antithrombin, thus liberating prothrombin, which being activated by calcium forms thrombin. the principle which converts soluble fibrinogen into insoluble fibrin or clot. Kephalin, a purified brain lipoid, has been found to be an effective hemostatic when brought in contact with *oozing wounds* in hemophiliacs and others. Prepared after the method of Howell, it is soluble in ether, but insoluble in alcohol, acetone and water. Intramuscular injections of kephalin are not effective, probably because they form within the organism a compensatory amount of antithrombin, and intravenous injections are by no means devoid of danger. Several preparations of a sterilized extract of cattle brain in physiologic saline solution are marketed under the name of *thromboplastin*. As all of these extracts deteriorate with time, they should not be used after the expiration of the date stamped on the label of the container. If the prepared extracts are not at hand, good results may sometimes be achieved by the direct application of fresh tissues, such as brain, lung, etc.

The preparation marketed under the name of *Coagulen*, which is an extract of blood-platelets, may be given subcutaneously or applied locally.

Soluble Calcium Salts.—The chlorid and the lactate of calcium are available. The former (*Calcii Chloridum*, U. S. P.) occurs as white, deliquescent fragments, granules, or sticks, odorless and of a sharp saline taste. It is readily soluble in water. The dose is 8 to 15 grains (0.5–1.0 gm.), in solution, after meals. Calcium lactate (*Calcii Lactas*, U. S. P.) occurs as white granular masses or powder, odorless and nearly tasteless. It is soluble in about 20 parts of water. The dose is 10 to 30 grains (0.65–2.0 gm.), in powder or solution, after meals. It is much less irritant than the chlorid. Apart from its function of giving hardness to the bones and teeth, calcium apparently decreases the permeability of the blood and lymph vessels, and in excess, as after intravenous injection, depresses nervous and muscle structures, and is antagonistic to magnesium and sodium. It is also necessary for the coagulation of blood, as without it prothrombin cannot be converted into thrombin. On the advice of Sir Almroth Wright, whose experiments led him to believe that

calcium renders the blood more coagulable, calcium salts have been extensively employed in the treatment of various *hemorrhagic diseases*, but with very indifferent results. Except in *obstructive jaundice*, in which the blood calcium seems to enter into combination with the bile-pigments, calcium deficiency is rare. In this condition calcium chlorid, in doses of 100 grains (6.5 gm.) a day over a period of several days, may be of service in lessening the hemorrhagic tendency. The adjustment of the dose of calcium is a somewhat difficult matter, for an excess of the drug inhibits coagulation as much as a deficiency. Calcium salts have been used with some success in the treatment of *tetany*, both post-operative and spontaneous. The treatment is based upon the researches of MacCallum and Voegtlin, who found that intravenous injections of a 5 per cent. solution of calcium lactate caused an almost immediate arrest of the tetanoid symptoms resulting from parathyroidectomy. These observers concluded that the parathyroids control the retention of calcium. Success has been reported from the use of calcium chlorid or lactate in the prevention of *serum rashes*, and in the treatment of *urticaria*, *angioneurotic edema*, *frost-bite* and *hay fever*. The benefits are probably to be ascribed to the action of the drug in lessening the permeability of the vessels.

Gelatinum, U. S. P. (Gelatin).—Gelatin is the air-dried product of the action of boiling water on gelatinous animal tissues, such as skin, tendons, ligaments, and bones. It occurs in brittle, transparent sheets or shreds, without odor or taste. It is insoluble in cold water, but freely so in hot water, and if the solution contain more than 2 per cent. it solidifies on cooling. Solutions heated above a temperature of 230° F. (110° C.), however, remain permanently liquid. A mixture of equal parts of gelatin and glycerin is known as glycerinated gelatin (*Gelatinum Glycerinatum*, U. S. P.). It is used for making vaginal suppositories, etc.

In 1896 Dastre and Floresco demonstrated that blood drawn from a dog into which a 5 per cent. solution of gelatin had been injected intravenously solidified almost immediately, and further that the same result could be secured by adding gelatin to the blood outside of the body. That the solidification was due to clotting and not merely to jellifying was evident from the fact that it occurred at a temperature (38° C.) at which a 5 per cent. solution of gelatin will not jellify, and, moreover, that it occurred also with solutions containing a percentage of gelatin much under that which is necessary for jellifying—that is, under 2 per cent. These observers also showed that gelatin could offset the anti-coagulant action of peptones, but not of concentrated saline solutions or of substances which decalcify the blood, like oxalic acid.

In 1898 Lancereaux and Paulesco found that subcutaneous injections of gelatin were as efficient in increasing the coagulability of the blood as intravenous injections. Whether or not its power is affected by digestion has not been definitely determined, although a number of practitioners have attributed good results in hemorrhage to its administration by the mouth or rectum. No satisfactory explanation has yet been offered of the action of gelatin in promoting the coagulability of the blood.

Locally, in the form of a 10 per cent. solution applied on tampons, gelatin has been used with some success in *epistaxis*, *bleeding from hemorrhoids*, *oozing from wounds*, etc. The drug has been used also subcutaneously in *hemoptysis*, *enterorrhagia*, *purpura hemorrhagica*, etc. and in *aortic aneurysm*, but the injections are painful and the treatment is of doubtful value. The dose for subcutaneous injection is from 15 to 40 grains (1.0–2.5 gm.), in 2 to 5 per cent. solution, once a day. It is important that the solution should be absolutely sterile, since gelatin not rarely contains tetanus bacilli and a number of cases of tetanus have been reported from the administration of the drug subcutaneously.

Gelatin makes a good protective dressing for *indolent leg ulcers*, especially when they are accompanied by chronic eczema. It may be employed in the form of Unna's dressing:

R. Zinci oxidi
 Gelatini..... āā 3j (4.0 gm.)
 Glycerini
 Aquæ..... āā f℥iv (120.0 mls).—M.

Sig.—After the ulcer has been thoroughly cleansed and disinfected, coat the eczematous regions with Lassar's paste (starch and zinc oxid, of each, 2 parts; vaselin, 4 parts), dust the ulcer with iodoform, and cover it with cotton. Then paint the entire limb with Unna's dressing, melted and applied with a brush. Bandage evenly and firmly, first with gauze soaked in hot water, then with dry gauze, and finally with a cotton roller bandage. The dressing should be changed every two, four, or six days, according to the amount of discharge.

Incompatibles.—Tannin, phenol, and formaldehyd.

GERMICIDES, ANTISEPTICS AND DEODORANTS

Germicides or disinfectants are agents that destroy bacteria. They may act by precipitating bacterial proteins, by entering into chemical or physico-chemical combination with bacterial constituents, by dehydration, or by changing the chemical composition of the medium containing the bacteria. It must be borne in mind that all germicides are much more powerful in the

test-tube under favorable conditions than in the presence of organic matter, such as blood-serum. The most important germicides are:

SALTS OF HEAVY METALS		{ Mercuric chlorid Silver nitrate
BENZENE (C_6H_6) DERIVATIVES		{ Phenol Cresols Guaiacol Salicylic acid Benzoic acid Naphthalin Betanaphthol
HALOGENS		{ Chlorin Iodin Bromin
Formaldehyd		
Sulphur dioxid		
Hydrogen dioxid		
Potassium permanganate		
Calcium oxid (Quicklime).		

The various salts of *quinin* also possess moderate germicidal power; they are especially destructive to certain protozoa, such as the hematozoa of malaria and the amebæ of dysentery. Derivatives of *hydrocuprein* have actions similar to those of quinin, but are more actively bactericidal. Organic arsenic compounds, especially *arsphenamin*, and salts of *antimony*, while comparatively feeble bactericides, are effective, when administered intravenously, in combating infections that are due to protozoan parasites, such as syphilis, frambesia, relapsing fever, kala-azar, etc. *Emetin*, an alkaloid of ipecac, is useful in amebic dysentery but whether it owes its efficacy to an amebicidal action is doubtful, as it is not very destructive to the organisms themselves *in vitro*.

HEAT is the most certain disinfectant. Virtually all bacteria and their spores are destroyed by boiling water within half an hour, and by steam ($212^{\circ}F.-100^{\circ}C.$), at ordinary pressure, within an hour. Steam under pressure is still more energetic, destroying nearly all organisms within a few minutes. Dry heat, on account of its slight penetrating power, is much less effective than moist heat. According to Koch, sporeless bacteria are destroyed in one and one-half hours by hot air at a temperature slightly above $212^{\circ}F.$ ($100^{\circ}C.$), and spores of bacilli in three hours by hot air at a temperature of $316^{\circ}F.$ ($140^{\circ}C.$).

Antiseptics are agents that prevent or hinder the growth of microorganisms without necessarily destroying them. Whether a substance acts as a germicide or as an antiseptic depends largely upon the degree of concentration in which it is employed. By dilution germicides may be reduced to the rank of antiseptics. The following substances may be classed as antiseptics, since in the solutions ordinarily used they retard the growth of bacteria, but do not destroy them:

Resorcinol	
Boric acid	
Picric acid	
Ferrous sulphate	
Many volatile oils	{ Eucalyptus
	{ Thyme
	{ Sandalwood
	{ Copaiba
Many anilin derivatives	{ Cubeb
	{ Methyl-blue
	{ Methylene-blue
	{ Acetanilid.

Deodorants are agents that destroy offensive odors. They do not, of necessity, possess either germicidal or antiseptic power. They may act by oxidizing or deoxidizing fetid compounds or by abstracting hydrogen from them. The most powerful deodorizers are:

Chlorin	Sulphur dioxid
Formaldehyd	Potassium permanganate
Calcium oxid (Quicklime)	Hydrogen dioxid
Charcoal.	

Pulverized dry **earth** is a useful deodorant of fecal matter but it is not to be considered as a disinfectant.

General Surgical Antisepsis.—Mercuric chlorid (see p. 391) is the most popular of the germicides for general surgical work. It is energetic, soluble, and cheap. On the other hand, it has three disadvantages: it is very poisonous, it is destructive to metal instruments, and it is readily converted into an inert compound in the presence of albuminous matters. This last drawback may be offset by adding to its solutions a weak acid (tartaric acid). For the patient's skin and the surgeon's hands solutions of from 1:1000 to 1:500 should be employed; for large wounds and cavities, 1:10,000 to 1:5000; and for small wounds, 1:2000. On account of its irritant properties, it should not be used on serous membranes.

Phenol is not so reliable as corrosive sublimate, but it is quite destructive to pus-organisms. It is readily soluble, is not affected by albuminous matters, and does not seriously injure metal instruments, although it dulls them. On the other hand, it is decidedly toxic, and it has a benumbing effect on the hands of the operator. A solution of 1:20 is often employed for cleansing suppurating wounds, sinuses, and abscess cavities. A solution of 1:40 is sometimes used as a bath for instruments.

Certain chlorin antiseptics, such as dilute hypochlorite solutions, are actively germicidal, are only slightly irritant, are virtually non-toxic, and have a solvent action on dead tissue. They have been found especially useful in the treatment of infected wounds by the saturation technic of Carrel and for irrigating abscess cavities, etc.

Formaldehyd is a very powerful germicide, but it is too irritant to be generally useful in surgical work. One or 2 per cent. solutions of liquor formaldehydi (37 per cent. of the gas in water), however, are sometimes employed to disinfect wounds and to irrigate sinuses and suppurating cavities. Instruments may be disinfected by immersion in a 2 per cent. solution of formalin, or, better, by subjecting them to the action of the gas in a closed chamber (see p. 434).

Disinfection of the Hands.—Fürbringer's method, or some modification of it, is usually followed: After removing all dirt from around and beneath the nails, the forearms, hands, and nails are thoroughly scrubbed with soap and hot water. The hands are then soaked for at least a minute in alcohol (95 per cent.), and before the alcohol has evaporated they are plunged in a hot solution of corrosive sublimate, 1:500. Finally, they are rinsed in sterile water and dried. The alcohol removes the soap and grease from the furrows and pores, and favors the penetration of the germicide. Kelly, after scrubbing the hands, dips them in a warm, saturated solution of potassium permanganate, then in a warm, saturated solution of oxalic acid, and, finally, in distilled water. Weir's method has been found very satisfactory. It is applied as follows: Scrub the hands and forearms in running hot water, using a brush and green soap; clean under and around the nails with a bit of soft wood; place in the palm a tablespoonful of chlorinated lime and an equal quantity of washing soda (not sodium bicarbonate); add enough sterile water to make a creamy mass, and rub this cream over the hands and forearms until the harsh soda granules can no longer be felt. This rubbing should occupy about five minutes. Push the paste under and around the nails by means of a piece of sterile orange-wood, and then wash in hot, sterile water.

Antisepsis of Mucous Membranes.—The most important bacterial poisons for use on mucous membranes are mercuric chlorid, silver nitrate, organic silver compounds, boric acid, potassium permanganate, hypochlorite preparations, and solution of formaldehyd.

Gastrointestinal Antisepsis.—Internally, antiseptics are apparently of service in lessening fermentation and putrefaction in the contents of the stomach and bowel. Of course, they cannot render the alimentary canal aseptic, nor can they affect bacteria, such as the typhoid bacillus and the tubercle bacillus, which multiply in the intestinal walls. The chief gastrointestinal antiseptics are phenol, creosote, guaiacol carbonate, naphthalin derivatives, salicylic compounds, sulphites, resorcin, and thymol. Bismuth subnitrate, silver nitrate and the mercurial preparations also owe, no doubt, some of their efficacy in affections of the digestive tract to their antiseptic properties. It must be borne in mind that any antiseptic may actually increase the intestinal flora if given in doses sufficiently large to irritate the mucous membrane of the bowel. The conclusions of Friedenwald and Leitz that "regulation of diet, together with the evacuation of the bowels, is the most effectual method that we have at hand of reducing the excessively high bacterial content of the large intestine" is probably not far from the truth.

Urinary Antiseptics.—It is quite possible to inhibit the growth of microorganisms in the urine by administering antiseptic agents by the mouth. Hexamethylenamin, salicylic compounds, benzoic acid, and several volatile oils (copaiba, cubeb, sandalwood) are used for this purpose.

Internal Antisepsis.—Thus far no general infection excited by a micrococcus or bacillus has been successfully treated by the internal administration of any of the ordinary germicides. In every case the disinfecting agent has shown a greater tendency to attach itself to and destroy the tissues of the host than to attack and kill the parasites; that is, its action has been organotropic rather than parasitotropic. A number of human and animal diseases caused by protozoa and spirilla, however, have been successfully treated by chemical compounds. Thus, quinin has been found to be curative in malaria, mercury and arsenic in syphilis, arsenic in frambesia or yaws, antimony in kala-azar, and emetin in amebic dysentery.

Disinfection of Stools and Sputum.—Stools should be thoroughly mixed with twice their volume of a 3 per cent. chlorinated lime solution, of a 5 per cent. phenol solution, or of a 5 to 10 per cent. formalin solution (37 per cent. formaldehyd), allowed to stand for two or three hours, and then buried or dis-

charged into the closet. Infected sputum should be received into cups containing a 3 per cent. chlorinated lime solution or a 5 per cent. phenol solution; or the patient may expectorate into moist rags or into impermeable paste-board cups, which should be burnt before the sputum has had time to dry.

Disinfection of Rooms and Their Contents.—Articles of little value should be burnt. Bedding, clothing, carpets, etc., should be disinfected by steam. Towels, napkins, and sheeting should be soaked in a 5 per cent. phenol solution and then boiled. Woodwork, floors, and plain furniture should be washed with a chlorinated lime solution (1 per cent.) or with a corrosive sublimate solution (1:5000). Finally, the room should be fumigated with formaldehyd gas (see p. 433) or with sulphur dioxid (see p. 437), preferably with the former. Recent investigations have shown that infection in such diseases as scarlatina, diphtheria and smallpox is chiefly by direct transmission and that the organisms responsible for these diseases soon die outside of the body; consequently gaseous disinfection of rooms has been abandoned as a prophylactic measure in many of the larger cities.

HYDRARGYRUM

(Mercury, Quicksilver, Hg)

Mercury is a heavy, liquid metal, of a silvery luster, and without odor or taste.

Pharmacologic Action.—Mercury is a general protoplasmic poison. The soluble mercuric salts (corrosive sublimate) form albuminates with proteins and are intensely irritant. They are active germicides, although they lose much of their effectiveness in this respect in the presence of the proteins of the body fluids. The insoluble mercurous salts (calomel) are without irritant or germicidal properties. In the bowel, however, a sufficient amount of calomel goes into solution to stimulate peristalsis and produce a cathartic effect and to lessen intestinal putrefaction. In dropsical conditions calomel may also excite pronounced diuresis, but whether this effect is an indirect one, the result of the action of the drug on the intestine, or is due directly to an action exerted on the kidney itself is not known. All mercurial preparations are antisymphilitic, probably by acting directly on the *Spirochæta pallida*. As they have a greater tendency to destroy the parasite of syphilis than to injure the tissues of the host, they are characteristically parasitotropic (see p. 386). If given early in the disease, organic arsenic (arsphenamin)

alone may be sufficient to effect a cure, but in the majority of cases courses of mercury in some form are indispensable.

Both soluble and insoluble compounds of mercury, and even metallic mercury itself, are readily absorbed. Excretion occurs by all channels, but chiefly by the large intestine and the kidneys, and not rarely in acute poisoning these organs show relatively greater damage than the stomach, which bears the brunt of the drug's local corrosive action. Excretion begins in a few hours after absorption, but proceeds slowly and somewhat irregularly and after repeated administrations traces of the metal may be found in the urine or feces for many weeks. Owing to its tardy excretion, mercury is prone to produce cumulative effects.

Toxicology.—**ACUTE POISONING.**—The most acute form of mercurial poisoning is that resulting from swallowing tablets or a solution of corrosive sublimate. The symptoms usually appear within half an hour and consist of a metallic and astringent taste, severe abdominal pain, vomiting and purging of mucous and bloody material, and signs of collapse. Corrosion of the mouth or throat may also occur. Unless death ensues within a few hours, which is exceptional, symptoms of acute stomatitis (salivation, congestion, and swelling of the gums, etc.), of acute colitis (bloody diarrhea with tenesmus) and of acute nephritis (oliguria or anuria, albuminuria, etc.) usually supervene. Occasionally, neither the nephritic nor the dysenteric features show themselves for several days or until there has been complete recovery from the corrosive effects of the drug. Death usually occurs within a week, but sometimes slow recovery ensues even after anuria has lasted for several days.

Postmortem examination shows corrosion and inflammation of the alimentary canal, sometimes with membranous colitis; acute nephritis, often with calcareous "infarcts" in the uriniferous tubules; and degenerative changes in the other solid organs.

Treatment.—Egg-white should be given at once to precipitate any mercuric chlorid that has not yet entered the duodenum, and then the stomach should be emptied, preferably by the stomach-tube. To remove the poison from the bowel the gastric lavage should be followed by the administration of Epsom salt (1 ounce—30.0 gm.), and by irrigation of the colon. It is advisable to repeat the enteroclysis twice daily as the mercury is excreted chiefly by the colon. Hot packs and alkaline diuretics, with large drafts of water, are of service in promoting elimination through the skin and kidneys respectively. Lambert and Patterson recommend hourly liquid by the mouth, 8 ounces (240.0 mls) of milk, alternating with 8 ounces (240.0 mls) of the following mixture:

Potassium bitartrate	
Sugar, of each.....	℥j (4.0 gm.)
Lactose.....	℥iv (15.0 gm.)
Lemon juice.....	f℥j (30.0 mls)
Boiled water, to make.....	Oj (480.0 mls).

In anuria repeated flushing of the colon with hot water, 110° F. (44° C.) and intravenous injections of saline solution should be tried. In a few instances decapsulation of the kidneys has been successful.

SUBACUTE POISONING.—This is observed most frequently as a result of the use of mercury for medicinal purposes, the doses being too large or the treatment too long continued, but it is also seen in sequence to acute poisoning. The most conspicuous feature is stomatitis, which is probably due partly to the direct irritant action of mercury that is excreted in the mouth, partly to the precipitation of mercuric sulphid in the capillary endothelium (Almkvist), and partly to secondary infection. The susceptibility to mercurial stomatitis varies greatly. It is increased by poor hygienic conditions of the mouth and teeth and by chronic nephritis. Even a grain of calomel has been known to produce it. The earliest symptoms are a metallic taste, salivation, fetor of the breath, and redness and soreness of the gums. If the administration of the drug is continued glossitis develops with marked swelling of the tongue, the gums become spongy and ulcerated, the salivary glands enlarge, the teeth loosen and fall out, and finally necrosis of the maxillary bones ensues. At the same time the general health is more or less affected. The patient becomes pale and loses flesh, fever, chilliness, thirst and anorexia not rarely occur, and after a time symptoms of colitis and of nephritis may supervene.

Treatment.—The administration of mercury should be suspended as soon as the slightest tenderness of the gums appears. The mouth should be rinsed at frequent intervals with a saturated solution of potassium chlorate or alternately with this and a solution of hydrogen dioxid (1 to 3 of water). In severe cases the affected parts may be painted with a solution of argyrol (20 per cent.) or a solution of silver nitrate (5 to 10 per cent.). To check the excessive flow of saliva, atropin sulphate, $\frac{1}{125}$ of a grain (0.0005 gm.), may be given once or twice a day. Morphin is sometimes required at night to relieve pain and produce sleep. Later, tonics may be of service in combating anemia and exhaustion.

CHRONIC POISONING.—This is observed chiefly in workmen who handle mercury or who are exposed to its fumes. Thus, it occurs in makers of mirrors, thermometers, barometers, incan-

descent electric bulbs, felt hats, and explosives derived from fulminate of mercury. Occasionally, it is induced by the prolonged use of mercury as a medicine. Its chief manifestations are stomatitis with salivation, gastrointestinal disturbances, muscular weakness, emaciation, cachexia, and various nervous and psychic disorders, especially tremors and mental impairment, with irritability and depression. Multiple neuritis has also been described, but according to Starr, no case can be found which is not open to objection.

Treatment.—Removal of the patient from exposure to the mercury is imperative. Tonics are usually indicated. Free water drinking, active catharsis and warm baths are useful in promoting elimination. The administration of potassium iodid is also recommended, but it is of doubtful value.

Untoward Effects.—Certain persons are exceedingly susceptible to the influence of mercury. One grain of calomel has been known to induce severe stomatitis. The presence of nephritis seems to diminish tolerance for the drug. An erythematous or eczematous rash occasionally follows the administration of mercury by the mouth or its application to the skin. Calomel should not be applied to mucous membranes or be taken internally while the patient is under the influence of potassium iodid, as the latter is eliminated in all secretions and readily forms with mercurous compounds the irritant mercuric iodid.

Therapeutics.—Mercury is used internally as an anti-syphilitic, cathartic, and diuretic, and externally as a disinfectant, parasiticide, absorbent and stimulant application.

Antisyphilitic.—Arsenic, mercury, and iodids are the remedies relied upon to combat *syphilis*. Mercury itself is effective in every stage of the disease, but it yields its best results when given in courses alternately with arsenic. The iodids are not destructive to the spirochetes of syphilis, nevertheless, they are of value in the later stages of the disease, especially when the bones, nerve-centers and internal organs are affected. It has been suggested that their resorptive action on the luetic exudate favors access of mercury or arsphenamin to the parasites (Longscope).

The preparations of mercury most frequently prescribed in syphilis are mercurous iodid, mercuric iodid, mercuric chlorid, mercury with chalk, mercuric salicylate, mercuric benzoate, mercurous chlorid and mercurial ointment. The drug is administered by the mouth (mercurous iodid, mercuric chlorid, mercuric iodid, mercury with chalk), by intramuscular injection (mercuric salicylate, mercurous chlorid, mercuric chlorid, mercuric benzoate), by inunction (mercurial ointment), and rarely

by intravenous injection (mercuric chlorid). Whatever the preparation or method of administration, the dose should be just short of that which produces toxic effects.

Cathartic.—Certain insoluble preparations of mercury—calomel, blue mass, mercury with chalk—have just enough irritant action on the intestine to induce catharsis. They are not suitable remedies for habitual constipation, but on account of their efficient and agreeable action, especially when followed by a saline, they are well adapted for unloading the bowel in the symptom-complex described as “*biliousness*,” in *dyspeptic diarrhea*, and at the *beginning of acute infectious diseases*.

Diuretic.—Mercury in the form of calomel or blue mass sometimes produces marked diuresis in *dropsy*, especially when this is due to cardiac disease. Some authorities advise against its use in nephritic edema, but while it often fails in this condition, the effects of the drug in appropriate doses are not likely to be bad.

Disinfectant.—While the soluble salts of mercury are effective germicides, they have certain drawbacks; thus, they are very toxic, they are irritant to the tissues, they are destructive to metal instruments, and they are readily precipitated by proteins. Nevertheless, they are favorite germicides for *general surgical work*. The bichlorid is the salt usually selected for the purpose.

Parasiticide.—Mercury is a valuable local remedy in certain parasitic infections of the skin, especially *tinea circinata* or *ringworm of the body* and *pediculosis pubis*. In the former a lotion of mercuric chlorid is usually employed, and in the latter mercurial ointment or an ointment of ammoniated mercury. In localized pustular skin diseases, such as the *impetigos* and *common sycosis*, ointments of ammoniated mercury are also of service.

Absorbent.—Ointments of mercury are sometimes of service in promoting absorption of the exudation in certain subacute or chronic inflammatory processes. For this purpose they have been used somewhat extensively in *adenitis*, *orchitis*, *arthritis*, *thecitis*, and *synovitis*. It need scarcely be added that they are without value in purulent inflammation.

Stimulant Application.—Owing to their stimulant properties, ointments of ammoniated mercury are often of benefit in *regional eczema* and other localized inflammatory conditions of the skin, when the process is subacute or chronic and characterized by sluggish infiltration.

HYDRARGYRI CHLORIDUM CORROSIVUM

(Mercuric Chlorid, Corrosive Sublimate, Bichlorid of Mercury, HgCl_2)

Mercuric chlorid occurs as heavy, colorless rhombic crystals, or crystalline masses, or as a white powder, odorless, and of an

acid metallic taste. It is soluble in 13.5 parts of water or in about 4 parts of alcohol. The dose is from $\frac{1}{24}$ to $\frac{1}{12}$ grain (0.0028–0.005 gm.).

PREPARATION

Toxibellæ Hydrargyri Chloridi Corrosivi, U. S. P. (Poison tablets of corrosive mercuric chlorid: Tablets of an angular shape and a blue color each having the word "poison" and the skull and cross bones design stamped upon it and consisting chiefly of $7\frac{1}{2}$ grains—0.5 gm.—of mercuric chlorid with sodium chlorid.) A tablet to a pint (0.5 L.) of water makes approximately a 1:1000 solution.

Therapeutics.—Mercuric chlorid is employed chiefly as a germicide, parasiticide, and antisyphilitic.

Germicide.—It is an energetic germicide, capable under favorable conditions of inhibiting the growth of most bacteria even in solutions of 1:20,000. Spores are much more resistant to its action, even a 1 per cent. solution being not certainly destructive to the spores of anthrax. In the presence of hydrogen sulphid it is converted into an insoluble and inert sulphid of mercury; with albuminous matter it forms an impermeable albuminate, which prevents its further penetration; it has a corroding action on metal; and when applied too freely to wounds or mucous membranes it may be absorbed in sufficient quantity to induce poisoning. Notwithstanding these drawbacks corrosive sublimate is well regarded by surgeons as a disinfectant for the *skin of the patient and the hands of the operator*. It is also used in cleansing *infected wounds and mucous membranes*, but much less extensively for this purpose than formerly. It should never be introduced into serous cavities or applied to aseptic wounds. Concentrations of 1:2000 to 1:1000 are employed for the skin; 1:2000 for small wounds; 1:10,000 to 1:5000 for large wounds and cavities; 1 to 10,000 to 1:5000 for the vagina; 1:40,000 to 1:20,000 for the urethra; and 1:5000 for the mouth and conjunctiva. In preparing the solution distilled water should be used, as the foreign matter in ordinary water tends to precipitate the mercuric salt. To prevent precipitation and to facilitate solution, sodium chlorid, ammonium chlorid, hydrochloric acid or citric acid is usually added to the corrosive sublimate, although the disinfectant power of the latter is somewhat impaired by the addition.

As a household disinfectant mercuric chlorid has several disadvantages. It is very poisonous; it has a corroding action on metals; it becomes ineffective by contact with albuminous matters; and it renders indelible any stains of feces or blood that may be on clothing. Solutions of from 1:5000 to 1:1000, however,

are serviceable for scrubbing floors, wood-work, and bare walls. It is not a suitable disinfectant for sputum, feces, or other excreta rich in albuminous matter.

Parasiticide.—As a parasiticide corrosive sublimate is a useful remedy in *pediculosis pubis* and *ringworm*. In these affections it may be employed in the form of a lotion in the strength of from 2 to 4 grains (0.13–0.26 gm.) to the ounce (30.0 mls) of water, or, better, tincture of benzoin.

Antisymphilitic.—Corrosive sublimate, though more irritant than the protiodid of mercury, is a reliable salt of the metal for administration by the mouth in *syphilis*. It may be given either in pill or solution. One-twentieth of a grain (0.003 gm.), gradually increased to $\frac{1}{12}$ grain (0.005 gm.) may be given three times a day, after meals. The addition of a small amount of opium will usually prevent colic. In the tertiary stage mercuric chlorid may be prescribed with potassium iodid, as in the following formula:

R̄.	Hydrargyri chloridi corrosivi.....	gr. j–ij (0.065–0.13 gm.)
	Potasii iodidi.....	ʒiv–vj (15.0–23.0 gm.)
	Syrupi sarsaparillæ compositi.....	fʒij (60.0 mls)
	Aquæ.....	q. s. ad fʒiij (90.0 mls).—M.

Sig.—A teaspoonful in water thrice daily, after meals.

Although it is very irritant, mercuric chlorid is sometimes administered by deep intramuscular injections. From $\frac{1}{10}$ to $\frac{1}{4}$ grain (0.0065–0.016 gm.) of the drug dissolved in normal salt solution is injected deeply in the muscles of the back or buttock daily, for a period of 5 or 6 weeks, unless some contraindication demands earlier discontinuance of the treatment. The advantages of intramuscular injections in syphilis are more prompt action, closer supervision of the treatment, and, in the case of the soluble preparations, more exact dosage. The chief disadvantages are the pain induced by injections and the possibility of abscess formation.

Occasionally, when a very rapid effect seems necessary, mercuric chlorid may be given intravenously, five or six injections of $\frac{1}{6}$ to $\frac{1}{3}$ grain (0.01–0.02 gm.), each in salt solution, being employed. Finally, in cerebrospinal syphilis, tabes, etc. bichlorid of mercury may be given in the form of mercurialized serum by intraspinal injection. Byrnes mixes 1.3 to 2.6 mg. of mercuric chlorid with 12 mls of human blood serum, adds 18 mls of normal saline solution, and then inactivates the mixture by subjecting it for an hour to a temperature of 58° C. (136° F.). He states that this clear mixture causes no irritation when injected into the subarachnoid space.

Incompatibles.—Mercuric chlorid has a wide range of incompatibilities. The most common substances precipitated by it are tannin, alkaline carbonates, albumin, iodids, silver nitrate, and solutions of lime. With potassium iodid it forms mercuric iodid, but if the potassium salt is present in excess, a colorless solution of the double iodid of mercury and potassium at once results, so that a combination of the two drugs is admissible.

Yellow wash (Lotio Flava) is made by adding 24 grains (1.6 gm.) of mercuric chlorid to 16 ounces (474.0 mls), of lime-water. Yellow mercuric oxid is precipitated and calcium chlorid remains in solution. It is sometimes employed as a stimulating dressing in the treatment of *phagedenic venereal sores*.

HYDRARGYRI CHLORIDUM MITE, U. S. P.

(Mild Mercurous Chlorid, Calomel, HgCl)

Calomel is a white, odorless, tasteless powder, insoluble in all ordinary menstrua. The dose is from $\frac{1}{10}$ to 10 grains (0.0065–0.65 gm.).

PREPARATION

DOSE

Pilulæ Catharticæ Compositæ, U. S. P. (each contains about 1 gr.

—0.06 gm. of calomel)..... 1–3 pills.

Therapeutics.—Calomel is used internally as a cathartic (see p. 229), as a diuretic (see p. 251) and as an antisyphilitic. Externally, it is employed as an antiseptic and stimulant.

Antisyphilitic.—Calomel has been used to some extent as an internal remedy in *syphilis*. For oral administration it is inferior to mercurous iodid, being more likely to cause diarrhea. Although mercuric salicylate (see p. 396) is preferable, calomel may be given by intramuscular injection. Of a 10 per cent. suspension in sterile liquid petrolatum, 10 minims (0.6 ml), which represent 1 grain (0.06 gm.) of calomel, may be injected into the gluteal region about twice a week for five or six weeks. In the treatment of syphilis by inunction, Schamberg, Kolmer, Raiziss and Gavron recommend that a calomel ointment be used instead of the ordinary blue ointment, as it is as readily absorbed through the skin as the latter and is less unclean. They suggest the following formula for each inunction:

R. Hydrargyri chloridi mitis..... gr. xlv (3.0 gm.)
 Adipis lanæ hydrosi..... gr. xv (1.0 gm.)
 Adipis benzoinati..... gr. xxx (2.0 gm.).

The local application of a 33 per cent. calomel ointment before and after infective contact has been used with considerable success in armies and navies as a preventive of syphilis (see p. 372).

Local Stimulant and Antiseptic.—Zinc ointment to which calomel, 5–15 gr. (0.3–1.0 gm.) to the ounce (30 gm.), has been added makes a useful application in *subacute* and *chronic eczema*.

℞. Hydrargyri chloridi mitis..... gr. v–xv (0.3–1.0 gm.)
 Phenolis..... gr. v–x (0.3–0.6 gm.)
 Unguenti zinc oxidi..... ℥j (30.0 gm.).

A dusting-powder composed of equal parts of calomel and zinc oxid is effective in *venereal warts*. Calomel is also efficacious in *corneal ulcers* and *phlyctenular conjunctivitis* when there is not much ciliary irritation. It should be flicked into the eye by gently tapping a camel's-hair brush loaded with the powder.

Incompatibles.—Calomel is incompatible with hydrochloric acid, chlorates, iodids, bromids, and lime-water. With hydrocyanic acid and potassium cyanid it forms the highly poisonous bicianid of mercury. Mixtures of calomel and iodoform turn red from the formation of mercuric iodid.

Black wash (Lotio Nigra) is made by adding 1 dram (4.0 gm.) of calomel to 1 pint (0.5 L.) of lime-water. Black mercurous oxid is precipitated and calcium chlorid remains in solution. It is sometimes employed as a stimulating application in *venereal sores*. It is often very useful in *rhus poisoning* and *acute eczema*, when dabbed on the parts, allowed to dry, and followed by an application of zinc ointment.

HYDRARGYRI IODIDUM RUBRUM, U. S. P.

(Red Mercuric Iodid, Biniodid of Mercury, HgI_2)

Red iodid of mercury is a bright-red, amorphous powder, free from odor and taste. It is almost insoluble in water, soluble in 115 parts of alcohol, and freely soluble in solutions of potassium iodid. The dose is from $\frac{1}{32}$ to $\frac{1}{12}$ grain (0.002–0.005 gm.).

PREPARATION

DOSE

Liquor Arseni et Hydrargyri Iodidi, U. S. P.

(Donovan's solution: 1 per cent. of each iodid). 1–5 min. (0.06–0.3 mil).

Therapeutics.—Mercuric iodid is rarely used except in the treatment of *syphilis*. It is usually prescribed in a solution of potassium iodid prepared by combining mercuric chlorid and potassium iodid in solution, as in the following formula:

℞. Hydrargyri chloridi corrosivi..... gr. ij (0.13 gm.)
 Potassii iodidi..... ʒvj (24.0 gm.)
 Syrupi sarsaparillæ compositæ..... f ʒiij (90.0 mils)
 Aquæ..... q. s. ad f ʒviij (240.0 mils).—M.

SIG.—One teaspoonful, increased to two teaspoonfuls, in water, after meals.

Donovan's solution has been used as an alterative in *chronic arthritis* and *tuberculous adenitis*.

HYDRARGYRI IODIDUM FLAVUM, U. S. P.

(Yellow Mercurous Iodid, Protiodid of Mercury, Green Iodid of Mercury, HgI)

Protiodid of mercury is a yellow, amorphous, insoluble powder, free from odor and taste. The dose is from $\frac{1}{10}$ to $\frac{1}{2}$ grain (0.006–0.03 gm.).

Therapeutics.—The protiodid of mercury is much less irritant than the biniodid. Ordinarily, it is the best preparation of mercury for administration by the mouth in *syphilis*. It is given in pill or tablet form after meals, the dose being gradually increased until the limit of tolerance is reached, and then reduced one-half. If colic results, the drug may be combined with a small amount of opium.

HYDRARGYRI SALICYLAS, U. S. P.

(Mercuric Salicylate, $\text{HgC}_7\text{H}_4\text{O}_3$)

Mercuric salicylate is a white, slightly yellowish or slightly pinkish powder, without odor or taste. It is nearly insoluble in water or alcohol, but is soluble in solutions of alkalis. It is one of the best of the insoluble preparations of mercury for intramuscular injection in *syphilis*. A 10 per cent. (by weight) suspension in liquid petrolatum may be used, from 5 to 10 minims (0.3–0.6 mil) being injected about twice a week. The following mixture is also efficacious:

R̄. Hydrargyri salicylatis..... gr. 1 (3.0 gm.)
 Adipis lanæ hydrosi..... gr. xxx (2.0 gm.)
 Olei olivæ..... q. s. ad f ʒj (30.0 mls)

Sig.—Inject 5 to 10 minims (0.3–0.6 mil), twice a week.

HYDRARGYRI BENZOAS

(Mercuric Benzoate, $\text{Hg}(\text{C}_6\text{H}_5\text{COO})_2\text{H}_2\text{O}$)

Mercuric benzoate is a white, crystalline, odorless and tasteless powder, almost insoluble in water, but soluble in aqueous solutions of sodium chlorid, forming a double salt. It is a favorite preparation of mercury for intramuscular injection in the treatment of *syphilis*. A freshly made 1 per cent. solution in distilled water, with the addition of 2.5 per cent. of sodium chlorid, may be injected daily in doses of 30 to 45 minims (2.0–3.0 mls) with comparatively little pain.

HYDRARGYRI SUCCINIMIDUM

(Mercuric Succinimid, $\text{HgC}_8\text{H}_8\text{O}_4\text{N}_2$)

Mercuric succinimid is a white crystalline powder, soluble in 75 parts of cold water or in 300 parts of alcohol. It is comparatively non-irritant and does not precipitate albumin. The dose, by the mouth, is from $\frac{1}{6}$ to $\frac{1}{4}$ grain (0.01–0.015 gm.).

Mercuric succinimid has been used by intramuscular injection in the treatment of *syphilis*, from 8 to 15 minims (0.5–1.0 mil) of a 2.5 per cent. solution being given daily or every other day. It is less efficient, however, than the benzoate or salicylate of mercury. Injections of the drug have also been recommended in tuberculosis, but they are of doubtful value.

OLEUM CINERIUM

(Gray Oil)

Oleum cinerium is a 40 per cent. suspension of metallic mercury in oil. It is sometimes used in the treatment of *syphilis* by intramuscular injection. The dose is 4 minims (0.25 mil), once a week for five or six weeks. Absorption occurs much more slowly than with suspensions of mercuric salicylate.

HYDRARGYRI SUBSULPHAS FLAVUS

(Yellow Mercuric Sulphate, Turpeth Mineral, $\text{Hg}(\text{HgO})_2\text{SO}_4$)

Yellow mercuric sulphate is a lemon-yellow, odorless, and tasteless powder, sparingly soluble in water. The dose is from 2 to 3 grains (0.1–0.2 gm.), repeated once.

Therapeutics.—This preparation of mercury was formerly much used as an emetic, but it has been replaced by less poisonous and less irritant drugs.

MERCUROCHROM—220

This compound is the disodium salt of dibrom-oxymercury fluorescein, dibrom-fluorescein being an anilin dye. It occurs as iridescent green scales, which are freely soluble in water. The solution stains the skin a bright-red color, but the stain is easily removed by washing the part in a solution of sodium hypochlorite or a 2 per cent. potassium permanganate solution, followed by a 2 per cent. oxalic acid solution.

Mercurochrome is not precipitated by proteins, and according to Young, White and Swartz, who introduced it, is an energetic germicide with considerable penetrating power, and comparative freedom from irritant properties. These authors have found it

superior to organic silver compounds in *subacute* and *chronic cystitis* and in *gonorrheal urethritis*. In cystitis $\frac{1}{2}$ to 1 ounce (15.0–30.0 mls) of a 1 per cent. solution is injected in the bladder after the viscus has been thoroughly irrigated with distilled water, and is allowed to remain about an hour. In gonorrheal urethritis a 1 per cent. solution, increased later to 2.5 per cent., is injected into the urethra after a cleansing irrigation with sterile water, and in the case of anterior urethritis is allowed to remain in five minutes and in the case of posterior urethritis an hour. The most satisfactory results have been in chronic urethritis. The intense stain is a drawback to the use of the drug as an injection by the patient. Clapp has used a 2 per cent. solution with good results in *gonococcal ophthalmia*, and a moist dressing of 1 per cent. solution has been found effective in *chancroidal ulceration*. It is reported also to be efficient ($\frac{1}{2}$ to 2 per cent.) in disinfecting the throats of *diphtheria carriers*.

MASSA HYDRARGYRI, U. S. P. AND HYDRARGYRUM CUM CRETA, U. S. P.

Massa Hydrargyri, or blue mass, is a triturate of metallic mercury with honey of rose, glycerin, licorice, and althæa, containing 33 per cent. of the metal. The dose is from $\frac{1}{2}$ to 10 grains (0.03–0.6 gm.). It is employed as a cathartic and diuretic. In the condition known as "*biliousness*" no treatment is so successful as the administration of a blue pill (5 gr.–0.3 gm.), followed in the morning by Epsom salt or a Seidlitz powder. In the beginning of *acute febrile diseases* and *dyspeptic diarrhea* blue mass is an excellent cathartic for unloading the bowel without inducing irritation. In combination with powdered digitalis and squill it is an efficient diuretic in the dropsy of *chronic heart* and *liver disease*.

Hydrargyrum Cum Creta, or mercury with chalk, is a light-gray, damp powder, without odor, and of a sweetish taste. It contains 38 per cent. of mercury intimately mixed with chalk, honey, and water. The dose is from $\frac{1}{2}$ to 10 grains (0.03–0.6 gm.). It is used in the same class of cases as blue mass. It is particularly serviceable in the *diarrhea of children* when the tongue is heavily coated, the breath fetid, and the stools are greenish or clay-colored. Hutchinson highly recommends mercury with chalk, in doses of from 1 to 4 grains (0.065–0.26 gm.), thrice daily, as a convenient and efficient form in which to administer mercury in syphilis. In *congenital syphilis* from $\frac{1}{4}$ to 1 grain (0.016–0.065 gm.) may be given three times a day.

HYDRARGYRI OXIDUM

(Mercuric Oxid, HgO)

Mercuric oxid occurs in two forms: Yellow oxid (*Hydrargyri Oxidum Flavum*, U. S. P.) and red oxid (*Hydrargyri Oxidum Rubrum*, U. S. P.). Both are heavy, permanent, insoluble powders, odorless, and of a somewhat metallic taste. The yellow oxid is an impalpable powder; the red oxid is more or less crystalline. They are not used internally.

PREPARATIONS

Unguentum Hydrargyri Oxidi Flavi, U. S. P. (10 per cent.)

Oleatum Hydrargyri, U. S. P. (25 per cent. of yellow oxid).

Therapeutics.—The oxids of mercury are used externally for their stimulant and alterative effects. In certain *chronic inflammatory diseases of the eye*—phlyctenular conjunctivitis, keratitis, and blepharitis marginalis—an ointment of the yellow oxid is often very useful. In the last affection it is particularly efficacious when applied at night to the margins of the lids in the strength of 1 grain of the oxid (0.06 gm.) to 1 dram (4.0 gm.) of vaselin. In *chronic eczema* an ointment containing from 10 to 20 grains (0.6–1.3 gm.) to the ounce (30.0 gm.) is sometimes serviceable. In the form of a dusting-powder, the oxids of mercury have also been used in *chancroidal* and *syphilitic sores*. In *chronic adenitis* and other *indolent inflammatory indurations* the ointment of the yellow oxid or the oleate may be employed for its sorbefacient effect.

The red oxid may be used in the same class of cases as the yellow oxid, but it is less satisfactory on account of its crystalline character.

HYDRARGYRI NITRAS

(Mercuric Nitrate, $\text{Hg}(\text{NO}_3)_2$)

Mercuric nitrate is employed in two forms:

Liquor Hydrargyri Nitratis (contains 60 per cent. of mercuric nitrate and 11 per cent. of free nitric acid).

Unguentum Hydrargyri Nitratis, U. S. P. (citrine ointment: contains 7 per cent. of mercuric nitrate).

Therapeutics.—The solution of mercuric nitrate is a powerful caustic. It is no longer official, but it is sometimes employed for the cauterization of *mucous patches* and *sloughing venereal sores*. The danger of inducing salivation from using it

too freely must be borne in mind. Citrine ointment, more or less diluted, may be used as a stimulant application in *indolent ulcers* and *chronic eczema*. Diluted with 8 parts of petrolatum it makes an efficient application for *granulating venereal ulcers*.

UNGUENTUM HYDRARGYRI

(Ointment of Mercury)

The U. S. Pharmacopœia recognizes two ointments of mercury: Mercurial ointment (*Unguentum Hydrargyri*) and blue ointment (*Unguentum Hydrargyri Dilutum*). Mercurial ointment contains 50 per cent. of metallic mercury and 2 per cent. of oleate of mercury in suet and lard; and blue ointment contains approximately 30 per cent. of metallic mercury in petrolatum, suet and lard. These preparations are employed as antisypilitics, absorbents, and parasiticides. In *sypilis* they are administered by inunction, which is a safe and satisfactory method of introducing large amounts of mercury into the system, although unclean and somewhat prone to irritate the skin. One dram (4.0 gm.), more or less, of mercurial ointment should be rubbed into the skin with a gloved hand once a day, each succeeding inunction being made in a different place to avoid irritation. The axillæ, the inner side of the arms, the groins and the inner side of the thighs are suitable regions for the applications. After the rubbing, which is best done at night, the patient puts on his underclothes and goes to bed, and in the morning takes a bath. In infants 5 to 10 grains (0.3–0.65 gm.) of mercurial ointment should be rubbed in daily for 10 minutes, after the part has been washed with soap and hot water and dried.

In *synovitis*, *bursitis*, *arthritis*, *glandular enlargements*, and *sypilitic nodes* the ointments of mercury are useful absorbents. If the swelling is painful, an equal amount of belladonna ointment may be added for its sedative effect. In *subacute infective arthritis* the local application to the affected joints of an ointment containing mercury and salicylic acid is sometimes beneficial.

- ℞. Acidi salicylici..... gr. xxx (2.0 gm.)
 Olei terebinthinæ..... f ʒiiss (10.0 mls)
 Adipis lanæ hydrosi..... ʒss (15.0 gm.)
 Unguenti hydrargyri..... ʒj (30.0 gm.).—M.

SIG.—Apply with gentle friction night and morning.

In *pediculosis pubis* the parasites are quickly destroyed by rubbing into the affected parts a small amount of blue ointment.

HYDRARGYRUM AMMONIATUM, U. S. P.

(Ammoniated Mercury, Mercuric Ammonium Chlorid, White Precipitate, NH_2HgCl)

Ammoniated mercury is made by the action of ammonia on corrosive sublimate, and appears as a white, insoluble powder, free from odor and taste.

PREPARATION

Unguentum Hydrargyri Ammoniatum, U. S. P. (10 per cent.).

Therapeutics.—Ammoniated mercury is employed externally, in the form of an ointment, as a germicide or parasiticide and local stimulant. It is very effective in localized pustular skin diseases, especially the *impetigos* and *common sycosis*. The official ointment, however, is too strong for ordinary use, a strength of from 10 to 20 grains (0.65–1.3 gm.) to the ounce of cold cream or petrolatum being sufficient. The applications should be made thoroughly, but gently two or three times a day. In *ringworm* of the non-hairy surface an ointment of 20 to 40 grains (1.3–2.5 gm.) to the ounce (30.0 gm.) is usually curative. An ointment of 5 to 30 grains (0.3–2.0 gm.) to the ounce (30.0 gm.) of zinc ointment or cold cream is sometimes of service in *subacute* and *chronic eczema* and *psoriasis*, if the disease is limited to a few areas.

BENZOL

(Benzene, C_6H_6)

Benzol is a colorless, inflammable liquid, insoluble in water, soluble in about 4 parts of alcohol, and readily miscible with oils. It is the mother substance of all the coal-tar drugs. It must not be confused with benzin, which is petroleum ether. The dose of benzol is from 5 to 20 minims (0.3–1.3 mls).

Pharmacologic Action and Therapeutics.—Compared with many of its derivatives, benzol has little antiseptic power, is only moderately toxic, and is not antipyretic. Single, full doses are not usually followed by any obvious effect, other, perhaps, than nausea and eructations. When the drug is given repeatedly, however, it depresses and eventually destroys the blood-forming tissues, especially the bone-marrow. The leukoplasmic function is first affected and then the erythroplastic, the result being an aplastic anemia, with reduction of white cells, blood-platelets, and erythrocytes. Animals poisoned with benzol show after death not only destructive changes in the entire hematopoietic system, but also fatty changes in the liver

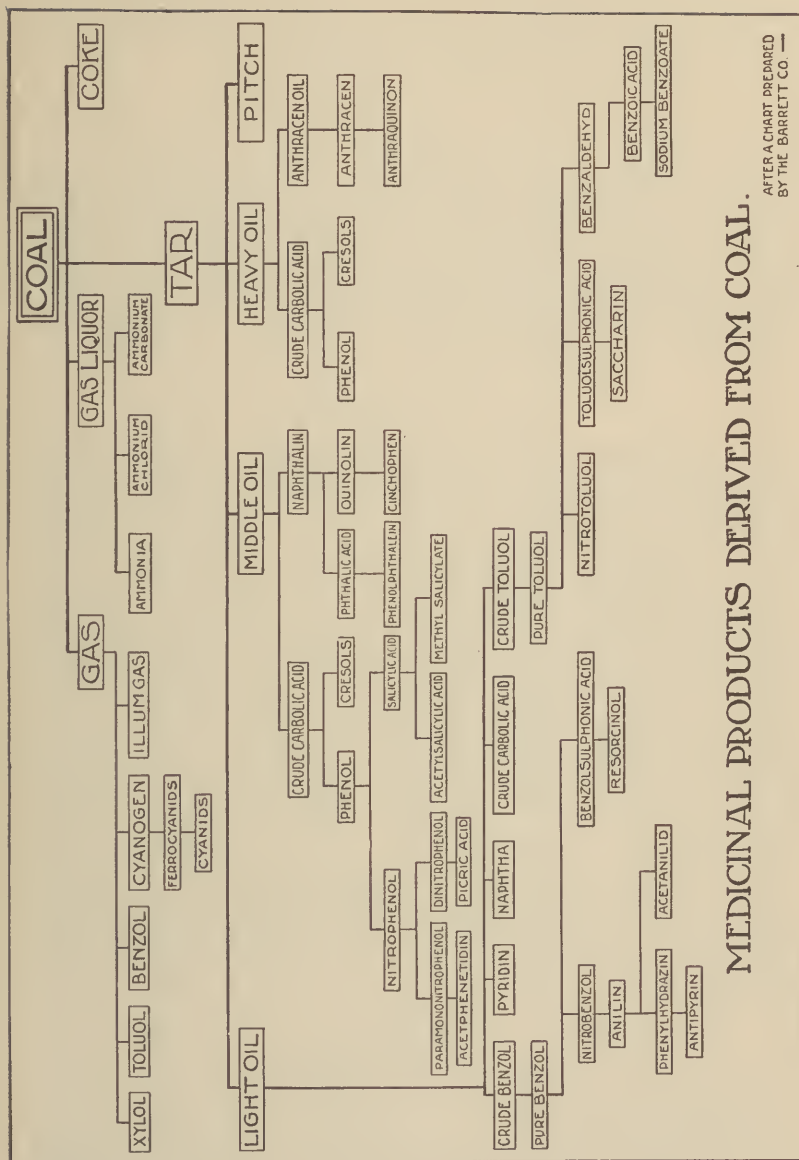
and kidneys, and hemorrhages into the mucous membranes. Poisoning is not uncommon in men who work in rubber, benzol being used as a solvent for this material. *Acute poisoning* is characterized by headache, vertigo, mental excitement, muscular twitchings, fever, coma and collapse; and *chronic poisoning* by gastrointestinal disturbances, dizziness, minute hemorrhages into the skin and mucous membranes, fever, leucopenia and anemia.

Benzol is partially oxidized in the body, and is excreted unchanged by the lungs and as phenol sulphates by the kidneys.

Benzol has been employed in medicine chiefly as a symptomatic remedy in *leukemia*. It reduces the number of leucocytes and sometimes brings about a temporary remission of the general symptoms, but its results are not uniformly favorable. The best method of administering the drug is in freshly filled capsules, with an equal amount of olive oil, the dose being cautiously increased from 10 minims (0.6 mil) to 20 minims (1.3 mils), three times a day. During the treatment the patient should be at rest and blood-counts should be made at frequent intervals. When the number of leucocytes has been reduced to 30,000 per cubic millimeter, the administration of the benzol should be immediately suspended, as the action of the drug persists for some time after its use has been discontinued. Persistent headache, digestive disturbances, vertigo, evidences of renal irritation, or the occurrence of anemia should also be regarded as a signal for the interruption of the treatment. The best results have usually been obtained by combining the use of benzol with x-ray or radium therapy.

Actions Shared by All Benzol Derivatives.—Nearly all benzol derivatives produce certain effects in common, the difference in the actions of the various members of the group being mainly one of degree. Locally, they are more or less irritant, antiseptic, and anesthetic; centrally, they are analgesic in headaches and neuralgias and antipyretic. Toxic doses, and even moderate doses in susceptible persons, tend to produce collapse by depressing the vasomotor system, and to produce cyanosis by transforming oxyhemoglobin into methemoglobin.

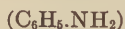
The *local irritant* effect is especially pronounced with phenol and pyrogallol (tri-hydroxybenzene); the *antiseptic effect* with naphthol, cresols, and phenol; the *antipyretic effect* with antipyrin, acetanilid, and acetphenetidin; the *analgesic effect* with the antipyretic group and the salicylates; the *collapse effect* with anilin, phenylhydrazin, and phenol; and the *effect on the blood* (methemoglobinemia) with nitrobenzol, anilin, phenylhydrazin. Certain members of the series are prone to produce in poisoning



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toxic jaundice. This is especially true of trinitrotoluene (T. N. T.), nitrobenzol and picric acid. Benzol, trinitrotoluene, and nitrobenzol in chronic poisoning also produce destructive changes in the bone-marrow, which result in *intense anemia*.

ANILIN



Anilin is benzol with one H atom replaced by an NH_2 group. It is not used for medicinal purposes, but it plays an important part in industrial poisoning. The chief symptoms of poisoning are cyanosis, dyspnea, increasing weakness, anemia, and mental impairment. Convulsions may also occur.

TRINITROTOLUENE



Trinitrotoluene represents benzol (C_6H_6) with 3 H atoms replaced by NO_2 and one H atom replaced by CH_3 . It has no therapeutic value, but it is used as a high explosive and poisoning by it is common among persons who are engaged in munition work. Absorption occurs chiefly through the skin. The earliest symptoms of poisoning are breathlessness, dizziness, mental depression, headache, nausea, colicky pains, and cyanosis. Irritation of the mucous membrane of the eyes, nose and bronchi, and eczematous lesions of the skin may also occur at an early period. Anemia gradually develops and eventually the number of red cells may be reduced to 1,500,000 or lower. Vomiting and diarrhea sometimes supervene, and in advanced cases jaundice, purpura, delirium, and other signs of acute degenerative hepatitis may appear.

The treatment of poisoning consists in withdrawing the patient at once from exposure to the offending compound, keeping him at rest in a well-ventilated room, securing free movements of the bowels with saline laxatives, and combating acidosis with alkalis.

NITROBENZOL



Nitrobenzol represents benzene with one H atom replaced by one NO_2 group. It is not used medicinally, but as it has the odor of bitter almond (hydrocyanic acid), it is used extensively as a cheap perfume for soaps, shoe-dyes, etc. Poisoning, which is often fatal, is characterized by weakness, nausea, breathlessness, cyanosis, headache, increasing anemia, and, finally, vomiting,

convulsions and coma. The cyanosis is usually very pronounced and in some cases it is accompanied by jaundice.

PHENOL, U. S. P.

(Phenol, Carbolic Acid, C_6H_5OH)

Phenol, or carbolic acid, is obtained from the distillation of coal-tar, and when pure occurs in the form of colorless, needle-shaped crystals of a characteristic odor and of an acrid, burning taste. In the light it acquires a reddish tint, and on exposure to the air it deliquesces. It is soluble in 15 parts of water, and freely in alcohol, glycerin, chloroform, ether, or oils. Although it combines with salifiable bases, it is chemically not an acid, but an alcohol of the benzene group (hydroxybenzene). The dose is from $\frac{1}{2}$ to 2 grains (0.03–0.13 gm.).

PREPARATIONS

DOSE

Phenol Liquefactum, U. S. P. (87 per cent. of absolute phenol and 13 per cent. of water) . . . $\frac{1}{2}$ –2 min. (0.03–0.12 mil)
 Unguentum Phenolis, U. S. P. (2.25 per cent.).
 Glyceritum Phenolis, U. S. P. (20 per cent.) . . . 2–10 min. (0.12–0.6 mil)

Pharmacologic Action.—**Local Action.**—When applied to the skin in concentrated form phenol produces a burning sensation, followed by numbness, and then a white eschar, which later becomes red and then brown. Finally, the eschar is cast off as a dry scab without the formation of pus. Alcohol, oils and glycerin lessen or prevent the corrosive action of phenol, as they have a much greater solvent affinity for the poison than the latter has for the fluids of the tissues. Dilute solutions of phenol merely produce numbness or hypesthesia. However, if the contact is prolonged, even dilute solutions (2–3 per cent.) may result in local gangrene. Phenol is readily absorbed from cutaneous surfaces, mucous membranes and wounds.

Action on Lower Organisms.—Phenol is fatal to most pathogenic bacteria, but is not very effective against spores. A solution of 1:1000 prevents the development of most bacteria; a solution of 1:100, under favorable conditions, destroys pyogenic cocci, tubercle bacilli, cholera bacilli, and many other non-spore-forming bacteria. Anthrax bacilli in the spore stage resist the action of a 5:100 solution for many days. Alcohol and ether as solvents lessen its germicidal power, and animal and vegetable oils, for which it has greater affinity than for the juices of tissues, destroy it. Heat increases its destructive action.

Systemic Action.—Qualitatively, phenol has actions similar to those of other benzol (C_6H_6) derivatives, such as acetanilid, salicylates, etc., but its antipyretic and analgesic effects are

fleeting and its collapse effects are dominant. Intravenous injections of even comparatively small doses, after slightly stimulating the heart and the vasoconstrictor center in the medulla, lower the bloodpressure. With toxic doses the respiratory center is also depressed and in fatal poisoning death is usually the result of asphyxia.

Excretion.—Phenol is excreted by all the emunctories, but chiefly by the kidneys. In the tissues a part combines with sulphuric and glycuronic acids, and is eliminated as the double sulphate and glycuronate of phenol; a part is oxidized into hydroquinon and pyrocatechin, which leave the body also largely as double sulphates and glycuronates. When the amount of phenol ingested has been very large, a small part may be excreted unchanged. After large doses the urine acquires a smoky or greenish-black color, which is due, probably, to oxidation products of hydroquinon and pyrocatechin. In poisoning ischuria and albuminuria are common symptoms.

Toxicology.—Poisoning may result either from the ingestion of the drug or from its external application. After the ingestion of a very large dose (1 oz.—30.0 mils) the usual symptoms are unconsciousness, contraction of the pupils, stertorous breathing, a rapid, feeble pulse and profound collapse. Muscular twitchings and even convulsions are occasionally observed. A significant feature is the rapidity with which death ensues. If the dose has not been so large, the systemic symptoms may be preceded by those of corrosion of the mucous membranes, namely, burning in the mouth and throat, abdominal pain, vomiting, etc. The characteristic phenomena are the odor of the drug on the breath, the white corrugated patches on the buccal mucous membrane, and the smoky urine. In poisoning from the use of phenol externally, the earliest symptoms are usually headache, vertigo, pallor and muscular weakness.

Treatment.—When the poison has been taken by the mouth, the stomach should be immediately washed out with water or a 20 per cent. solution of alcohol. None of the latter, however, should be allowed to remain in the stomach, as it is an excellent solvent of phenol and favors absorption. Sulphates have been recommended as antidotes, with the idea that they would form with phenol non-toxic phenolsulphonates, but they have not proved of value. Demulcents are useful in allaying local irritation, and the application of external heat and the intravenous or subcutaneous administration of diffusible stimulants and of salt solution are indicated.

Therapeutics.—As an antiseptic for general surgical purposes, phenol no longer holds a prominent place. Solutions

that are really effective are too irritant and too toxic to be employed. It is rarely used at present even for disinfecting instruments, because it dulls them and at the same time benumbs the surgeon's fingers. Its prolonged application in the form of a moist dressing, even in weak solution, is dangerous. Harrington collected 132 cases of gangrene of the fingers or toes from its external application. In most of these cases the strength of solution was less than 5 per cent. A solution of 1:20 is still employed to some extent for cleansing *suppurating wounds* and *abscess cavities*. *Carbuncles* are sometimes aborted by injecting into them in the early stage from 5 to 10 minims (0.3–0.6 mil) of a 10 per cent. solution. Excellent results have been obtained in *anthrax* from the injection of from $\frac{1}{2}$ to 1 dram (2.0–4.0 mils) of liquefied phenol into and around the eschar in the course of a day. Pure phenol is sometimes employed to destroy *chancroids* and *venereal warts* and to purify *sloughing wounds*.

A 5 per cent. solution may be used for disinfecting *soiled clothing* and *various excretions*, such as sputum, feces, and vomited matters. In the form of a 2 per cent. spray, it may be employed as an inhalation to destroy the fetor of the breath in such affections as *bronchiectasis* and *gangrene of the lung*.

Phenol is very useful as a local sedative and antipruritic. Carbolized oil, 10 grains (0.6 gm.) to the ounce (30.0 mils), although it has no antiseptic power, makes a soothing dressing for *superficial burns*. In the form of a lotion it is the most valuable remedy we possess to allay itching in *eczema*, *urticaria*, *jaundice*, and *pruritus*. It may be employed in the strength of from 2 to 3 drams (8.0–12.0 gm.) to the pint (0.5 L.), as in the following formula:

R. Phenolis.....	℥ij–iij (8.0–12.0 gm.)
Acidi borici.....	℥iv (15.0 gm.)
Alcoholis.....	f℥j (30.0 mils)
Glycerini.....	f℥ss (15.0 mils)
Aquæ.....	q. s. ad Oj (0.5 L.).—M.

Internally, phenol, in doses of $\frac{1}{2}$ to 1 minim (0.03–0.06 mil), is sometimes of service in controlling *vomiting* the result of gastric irritability. In the same doses, combined with bismuth subcarbonate, it may also prove useful as an antiseptic in *flatulent dyspepsia* and *diarrhea*, although creosote is usually preferable.

Administration.—For internal use, phenol may be prescribed in capsules, in powders with bismuth subcarbonate or subnitrate, or dissolved in some aromatic water.

Incompatibles.—Alkalis, metallic salts, soluble sulphates, collodion.

Sodii Phenolsulphonas, U. S. P. (Sodium Phenolsulphonate or Sodium Sulphocarbolate).—This salt occurs in colorless, rhombic crystals or crystalline granules, odorless, of a saline taste, and freely soluble in water. The dose is 2 to 5 grains (0.13–0.3 gm.). It is much less toxic and irritant than phenol and has been used chiefly as an intestinal antiseptic, but it is of little value.

Zinci Phenolsulphonas, U. S. P.—(Zinc Phenolsulphonate or Zinc Sulphocarbolate).—This salt has properties similar to those of sodium phenolsulphonate and has been used also as an intestinal antiseptic. The dose is 1 to 3 grains (0.06–0.2 gm.). A solution of 5 grains (0.3 gm.) to the ounce (30.0 mls) is sometimes used as a spray in *catarrhal affections of the throat* and as an injection in the second stage of *gonorrhea*.

Nosophen (*Tetra-iodo-phenol-phthalein*).—This compound is prepared by the action of iodine on a solution of phenolphthalein. It is a pale, yellow, inodorous, and tasteless powder. With bases it forms salts, the most important of which is the sodium salt (*antinosin*). It is recommended as an antiseptic dusting-powder.

Xeroform (*Tribromphenol-bismuth*).—This is a yellowish, odorless, tasteless, and insoluble powder, representing about 50 per cent. of bismuth oxid. It has been used in place of iodoform as an antiseptic application for infected wounds, burns, etc.

CREOSOTUM, U. S. P.

(Creosote)

Creosote is a mixture of phenols, chiefly guaiacol and cresol, obtained during the distillation of wood-tar, preferably of that derived from the beech tree. It is a colorless or yellowish oily liquid, having a penetrating, smoky odor, and a burning caustic taste. It is soluble in 150 parts of water, and miscible with alcohol, ether, or oils. The dose is from 1 to 10 minims (0.06–0.6 mil).

PREPARATION

DOSE

Aqua Creosoti, U. S. P. (about 1 per cent.) . . . 1–4 fl. dr. (4.0–15.0 mls).

Pharmacologic Action.—The action of creosote closely resembles that of phenol, but it is less toxic and irritant, and more antiseptic. Large doses produce all the phenomena of phenol-poisoning. The drug is excreted in large part by the kidneys and to a slight extent by the lungs.

Therapeutics.—Creosote is employed as an expectorant, an antiseptic, and a local anesthetic.

Expectorant.—Creosote and its derivatives are useful expectorants in *chronic bronchitis* and *bronchiectasis* with copious purulent sputum. So long ago as Addison's time, creosote was used as a remedy for pulmonary tuberculosis. This use was revived by Bouchard and Gembert in 1877, and again by Sommerbrodt in 1887. While it has been shown conclusively that the drug has no specific influence on the tubercle bacilli in the lung, nevertheless the testimony of numerous observers is convincing that it has a positive value in allaying cough, lessening expectoration, and lowering temperature. It should be given in small doses gradually increased, and at once withdrawn if the stomach shows any intolerance. Good results are seen only in tuberculosis attended with abundant sputum.

Antiseptic.—Creosote is sometimes of service as an internal antiseptic in *chronic gastric catarrh* with flatulence and in *simple dyspeptic diarrhea*. Creosote water has been recommended as a disinfectant lotion for *sloughing ulcers*, *uterine cancer*, etc., but for such a purpose it has no advantage over a dilute solution of phenol.

Local Anesthetic.—Inhalations of creosote are useful in allaying the cough of *laryngitis*, *bronchitis*, and *pulmonary tuberculosis*. Ten minims (0.6 mil) of creosote to 10 ounces (300.0 mls) of boiling water makes a good inhalation when the catarrh is acute. Doses of from 1 to 2 minims (0.06–0.1 mil) are sometimes efficacious in *vomiting* resulting from gastric irritability. In *toothache* a drop or two on a pledget of cotton may be inserted in the cavity of the tooth.

Administration.—The initial dose in tuberculosis should be small (1–3 min.—0.06–0.2 mil) and the amount gradually increased to 5 to 10 minims (0.3–0.6 mil), three times a day. The drug should be given after meals and withdrawn on the first appearance of any gastric disturbance. It may be taken in capsules or dissolved in a simple bitter, such as compound tincture of gentian. Intratracheal injections of creosote have been employed in pulmonary tuberculosis and chronic bronchitis, but guaiacol is preferable for this method of administration. In diarrhea, creosote may be prescribed in a powder of bismuth, as in the following formula:

℞. Creosoti..... ℥xij (0.75 mil)
 Morphine sulphatis..... gr. j (0.065 gm.)
 Bismuthi subnitrat. ʒss (15.0 gm.).—M.

Fiant chartulæ No. xii.

Sig.—One every three hours.

Incompatibles.—Strong nitric and sulphuric acids act violently upon creosote. It reduces silver salts and may explode when triturated with oxid of silver. It is also incompatible with ferric chlorid.

Creosoti Carbonas, U. S. P. (Creosote Carbonate, Creosotal). This is an oily liquid containing a mixture of the carbonates of the various phenols found in creosote. Its chief ingredient is guaiacol carbonate. It is odorless, of a slightly bitter taste, insoluble in water, but freely so in alcohol, ether, or fixed oils. It has pronounced advantages over creosote in having but little taste and in being more acceptable to the stomach. It may be employed in the same class of cases as creosote. Leyden and Cornet have highly recommended it in *pulmonary tuberculosis*. The dose is from 1 to 3 minims (0.06–0.2 mil), gradually increased to 10 to 20 minims (0.6–1.2 mils), thrice daily. It may be given in capsules or in milk, claret, or beef-tea.

GUAIACOL, U. S. P.



Guaiacol is the chief constituent of creosote, from which it is obtained by fractional distillation. It is a colorless, oily liquid, having a rather unpleasant aromatic odor and taste. It is slightly soluble in water, but freely so in alcohol or ether. It readily unites with acid radicals to form crystalline compounds. The dose is from 1 to 3 minims (0.06–0.2 mil), gradually increased to 10 minims (0.6 mil). It should be given in the same manner as creosote.

The action of guaiacol resembles that of phenol and creosote. In toxic doses it causes burning in the stomach, nausea and vomiting, brown-red urine, unconsciousness, and collapse. Wyss has reported a case of fatal poisoning in a girl of nine years from a dose of 80 minims (5.0 mils). It is absorbed and eliminated with great rapidity, undergoing partial oxidation in the body, and appearing in the urine as glycuronates and ethereal sulphates. When applied to the skin in sufficient quantity (20–30 min.—1.2–2.0 mils), evaporation being prevented, it causes in fever a marked fall of temperature. This antipyretic effect follows immediately upon its absorption, is attended with copious perspiration and depression, and is of comparatively short duration.

Guaiacol has been used internally as a substitute for creosote in *chronic bronchitis* and *pulmonary tuberculosis*, but it is now largely replaced by the more elegant carbonates of creosote and guaiacol. Charlton has found it very effective in relieving the

dysuria and increased frequency of urination attending *cystitis in elderly women*. He gives 5 to 10 drops after each meal. Intralaryngeal injections into the trachea of a mixture of guaiacol (1-2 per cent.) and olive oil are sometimes useful in *allaying cough* in chronic pulmonary diseases. From 10 to 20 minims (0.6-1.2 mils) of the mixture may be injected once or twice a day. Guaiacol cannot be recommended as an antipyretic, since its external application in typhoid fever, tuberculosis, and other infections is sometimes followed by profound exhaustion and even by collapse. The drug has proved of some value as a local anesthetic. In *epididymitis* and *orchitis* the gentle inunction of an ointment of guaiacol and lanolin (1:5), followed by the application of a snugly fitting suspensory bandage, affords much relief. In *laryngeal tuberculosis* an oily spray of guaiacol (20-40 per cent.) is sometimes useful.

Guaiacolis Carbonas, U. S. P.—This is an ester of guaiacol produced by the action of carbonyl chlorid on the sodium salt of guaiacol. It is a crystalline powder, odorless and tasteless, insoluble in water, and soluble in about 60 parts of alcohol. It is much less toxic than guaiacol or creosote and is usually well borne by the stomach. In the intestine it is slowly decomposed, liberating guaiacol. It is a useful expectorant in *bronchitis*, *bronchiectasis*, and *pulmonary tuberculosis* when the expectoration is abundant and purulent, having advantages over creosote in being free from odor and taste and in rarely disturbing digestion. The dose is from 5 to 10 grains (0.3-0.6 gm.), gradually increased, if necessary, to 20 grains (1.3 gm.). In doses of 10 grains (0.6 gm.), gradually increased to 20 grains (1.3 gm.), three times a day, it has been highly recommended by Luff and others in *rheumatoid arthritis*. As it undergoes decomposition in the intestine, it may be employed also as an intestinal antiseptic. It may be prescribed in capsules or powders.

R̄. Codeinæ sulphatis..... gr. iss (0.1 gm.)
 Guaiacolis carbonatis..... ʒiss (6.0 gm.)
 Terebeni..... fʒiss (6.0 mils)

Pone in capsulas No. xxx.

SIG.—Two capsules after meals. (*Subacute bronchitis*.)

Potassium guaiacolsulphonate (thiocol) and other esters of guaiacol, such as the benzoate (benzosol), cinnamate (styracol), and glycerol-ether (guaiamar) are sometimes employed, but they have no special advantages.

CRESOLS

The cresols, of which there are three—metacresol, orthocresol, and paracresol—are homologues of phenol. They are obtained

from coal-tar by fractional distillation, and are present in large quantity in crude carbolic acid. They closely resemble phenol in their action, but are more effective as germicides and less toxic. Their slight solubility in water is an important disadvantage. They are used chiefly for disinfecting specific excreta.

Under the name of *cresol* the U. S. Pharmacopœia recognizes a mixture of the three isomeric cresols obtained from coal-tar, and freed from phenol, hydrocarbons, and water. This preparation is a colorless or straw-colored liquid, having a creosote-like odor, and turning yellowish-brown on exposure to light. It is soluble in 60 parts of water, and miscible in all proportions with alcohol, ether, benzin, or glycerin. Its germicidal power is nearly three times greater than that of carbolic acid. A 1 per cent. solution may be employed in surgical work for the same purposes as carbolic acid. De Schweinitz recommends a 1 : 1000 solution as a solvent for atropin, cocain, and eserin in ophthalmic practice. Such solutions remain free from bacteria and are not irritant to the eye.

Liquor Cresolis Compositus, U. S. P.—This is a linsced-oil soap solution of cresol, of 50 per cent. strength. Aqueous mixtures containing from 3 to 5 per cent. of this official solution may be employed with advantage for disinfecting excreta. Mixtures of from 1 to 2 per cent. have been used rather extensively in obstetric practice. Injections containing from 0.5 to 1 per cent. have been found efficacious in *chronic cystitis*.

Creolin is the trade name of an emulsion of cresols prepared by means of rosin soap. It is a brownish, syrupy liquid, which, diluted with water, forms an opaque mixture.

Lysol is a cresol preparation made by dissolving in fat and subsequently saponifying with alcohol that portion of tar-oil which boils between 374° and 392° F. (190° and 200° C.). It is a brown, oily liquid, with the odor of creosote. It contains about 50 per cent. of cresols, and mixes with water to form a clear, saponaceous, frothy liquid. It may be used for the same purposes as the compound solution of cresol.

While the cresol preparations are comparatively safe, they are not altogether harmless. Poisoning from their absorption has not been very rare. There are many cases of poisoning by lysol on record.

THYMOL, U. S. P.

(Thymic Acid, $C_{10}H_{14}O$)

Thymol is a homologue of phenol obtained from the oil of thyme (*Thymus vulgaris*) and certain other volatile oils. It appears in the form of large, colorless crystals having the odor

of thyme and an aromatic pungent taste. It is only sparingly soluble in water, but freely so in alcohol, ether, or oils. The dose is from 1 to 10 grains (0.06–0.6 gm.).

PREPARATION

DOSE

Liquor Antisepticus (contains 0.1 per cent. of thymol)..... $\frac{1}{2}$ –2 fl. dr. (2.0–8.0 mls).

Pharmacologic Action and Therapeutics.—Thymol resembles phenol in its action, although it is decidedly less toxic and less irritant. It has been used as an antiseptic in the dressing of *wounds*, but its aromatic odor soon becomes disagreeable to the patient, and, moreover, is apt to attract flies. A solution of a grain (0.06 gm.) to the ounce of water (30.0 mls), a little alcohol being used as a solvent, makes a good mouth-wash in the infectious forms of *stomatitis* and *pharyngitis*. An ointment of thymol, 5 to 30 grains (0.3–2.0 gm.) to the ounce (30.0 gm.), has been used with some success by Crocker and others in chronic *eczema* and *psoriasis*. The drug makes an efficient lotion in *senile pruritus*.

Internally, thymol is sometimes used as an antiseptic in *sub-acute diarrhea*. In doses of 30 grains (2.0 gm.) for adults, or 8 to 15 grains (0.5–1.0 gm.) for children, repeated in two hours, it is a fairly efficient remedy (see p. 461) for *uncinariasis* or hook-worm disease, although its use has occasionally resulted in serious or even fatal poisoning. As alcohol and oils favor the solution and absorption of thymol, they should be withheld when large doses of the drug are being administered. It has also been used to some extent as a vermifuge against the *tapeworm* and *lumbricoid worm*. Thymol may be administered in wafers, capsules, or pills.

Thymolis Iodidum, U. S. P.—This compound, which is also known as *aristol*, is chemically dithymol-diiodid. It is prepared by acting upon thymol in alkaline solution with iodine dissolved in potassium iodid. It is an unstable preparation, containing about 45 per cent. of iodine, and appears as a brownish-red or reddish-yellow powder, tasteless and almost odorless. It is employed as a substitute for iodoform. Although it has advantages over the latter in being odorless and less toxic, it is generally not so efficacious.

RESORCINOL, U. S. P.

(Resorcin, Metadioxybenzol, $C_6H_4(OH)_2$)

Resorcin is a diatomic phenol, occurring in the form of colorless or faintly reddish prisms or needles having a slightly urinous

odor and a sweetish, pungent taste. It is readily soluble in water, alcohol, ether, or glycerin. The dose is from 1 to 3 grains (0.06–0.2 gm.).

Pharmacologic Action and Therapeutics.—Resorcin acts much like phenol, but it is less poisonous and less irritant. Toxic doses produce vertigo, ringing in the ears, tremors, epileptiform convulsions, quickening of the pulse and respiration, unconsciousness, and collapse. The urine becomes of an olive-green color.

At the present time resorcin is chiefly employed externally in certain diseases of the skin. It is a valuable remedy in *seborrhea*, especially in dandruff, in which disease it may be employed in the form of a 3 to 5 per cent. lotion, as in the following formula:

℞. Resorcinolis..... ʒiiss (6.0 gm.)
 Olei ricini..... ℥xx-xxx (1.2–2.0 mls)
 Spiritus myrciæ..... q. s. ad fʒiv (120.0 mls).—M.

A drawback to the use of resorcin on the scalp is its tendency when used over too long a period, especially during the summer months, to impart a reddish tinge to light hair. It is advisable, therefore to restrict its use to winter and for periods not exceeding two or three weeks.

A lotion containing from 5 to 20 grains (0.3–1.3 gm.) to the ounce (30.0 mls) is often serviceable in *subacute* and *chronic eczema*, especially of the vesicular variety. It is also a useful antipruritic remedy. According to Hartzell, its power to relieve itching is increased considerably by the addition of 0.5 per cent. of sodium chlorid to the solution, as in the following formula:

℞. Resorcinolis..... gr. xv-xxx (1.0–2.0 gm.)
 Sodii chloridi..... gr. xv (1.0 gm.)
 Glycerini..... fʒij (8.0 mls)
 Liquoris calcis..... q. s. ad fʒiv (120.0 mls).—M.

Internally, resorcin is occasionally used as an antiseptic in *chronic diseases of the stomach* and in *diarrhea*. It should be given in pill or capsule.

TRINITROPHENOL, U. S. P.

(Picric Acid, Carbazotic Acid, $C_6H_2(NO_2)_3OH$)

Picric acid is the product of the action of nitric acid on phenol-sulphonic acid, which is obtained by dissolving crystallized phenol in sulphuric acid. It occurs in yellow, flat crystals, odorless, and of an intensely bitter taste. It is sparingly soluble in water, but freely so in alcohol and in ether.

Pharmacologic Action and Therapeutics.—Locally, picric acid in pure form acts as a caustic. Poisonous doses produce

vomiting, diarrhea, yellowness of the skin, mucous membranes, and urine, convulsions, and collapse. As a germicide, it is more powerful than phenol.

Gauze wet with a 1 per cent. solution of picric acid, covered with cotton, makes an excellent dressing for *burns* of the first and second degree. For fear of poisoning, however, the dressing should not be applied over large or deep burns. The drug produces an anesthetic and antiseptic effect, and promotes epithelialization. A 1 per cent. solution applied to red areas on the skin is useful in *preventing bedsores*. A solution of the same strength has also been found efficacious in *herpes zoster*. A 6 per cent. solution in ethyl alcohol makes a good substitute for tincture of iodine in preparing the skin for operation. Occasionally local applications are followed by an erythematous rash. A saturated solution makes a delicate test for albumin in the urine.

ACIDUM SALICYLICUM, U. S. P.

(Salicylic Acid, $C_6H_4(OH)COOH$)

Salicylic acid is an organic acid contained in wintergreen, birch, and various other plants, but chiefly prepared artificially by acting on phenol with caustic soda and carbon dioxide. Chemically, it represents benzol (C_6H_6) with one H atom replaced by OH and another by the carboxyl radical, COOH. It occurs in fine white needles or as a crystalline powder, odorless, and of a sweetish, acid taste. It is soluble in 460 parts of water, 2.7 parts of alcohol or 3 parts of ether. The dose is from 5 to 20 grains (0.3–1.3 gm.).

Pharmacologic Action.—Salicylic acid resembles phenol qualitatively in its actions, but it is a more powerful antipyretic and analgesic and a less powerful poison and antiseptic. Single, moderate doses are not followed, as a rule, by any appreciable effects. Large doses, or even moderate doses, if frequently repeated, give rise to a sense of fulness in the head, headache, ringing in the ears, impairment of hearing, flushing of the surface, perspiration, and, not rarely, nausea and vomiting. In some cases an erythematous, urticarial or purpuric eruption also occurs. To this complex of symptoms, which closely resembles that resulting from large doses of quinine, the term *salicylism* has been applied. Toxic doses of salicylic acid or of salicylates produce, in addition to the usual phenomena of salicylism, amblyopia, albuminuria, delirium, deep and labored respiration, and finally unconsciousness and collapse. Death, which is usually the result of asphyxia, may be preceded by convulsions.

Local Action.—Local applications of salicylic acid to the unbroken skin lessen the secretion of sweat, and, if concentrated, exert a solvent action on the horny epithelium. In substance the drug is irritant and even slightly corrosive to mucous membranes and raw surfaces.

Action on Microorganisms.—Salicylic acid is only slightly less toxic for bacteria than phenol. The salicylates, however, are only feebly antiseptic.

Circulatory System.—Ordinary doses have but little effect on the general circulation, but toxic doses have the collapse action of all benzol derivatives. A moderate, but transient, leucocytosis is frequently observed after administration of the drug. In poisoning the red blood-corpuscles suffer disintegration.

Nervous System.—By affecting in some obscure way the sensory neurons, salicylates relieve headaches and neuralgic, muscular and articular pains. Of the benzol derivatives, they rank next in efficiency as analgesics to the antipyretic group (antipyrin, acetanilid, acetphenetidin). The sense of fullness in the head and the deafness occurring in salicylism are probably due to dilatation of the bloodvessels of the cerebrum and auditory apparatus respectively.

Digestive Organs.—Except in very weak concentrations, salicylic acid tends to retard the action of the digestive ferments. The drug is irritant to the stomach and even ordinary doses may cause nausea and vomiting. In large doses it appreciably increases the secretion of bile, but its power as a cholagogue is much inferior to that of bile itself or the salts of the biliary acids.

Metabolism.—Salicylates have a stimulating effect on protein metabolism and decidedly increase the output in the urine of uric acid. The increased elimination is accompanied by a decrease in the uric acid concentration of the blood and is probably due, as is the case with phenylcinchoninic acid (atophan), to a lowered threshold of the kidneys for uric acid.

Temperature.—In health the salicylic compounds have little or no influence on the body-temperature, but in fever they produce a marked antipyretic effect, which is probably of central origin, although immediately due, as is the case with the antipyrin group, to dilatation of the cutaneous vessels and augmentation of heat loss through sweating and increased radiation.

Absorption and Excretion.—Salicylic acid is rapidly absorbed from the digestive tract, from other mucous membranes, and even from the skin. It enters the blood as an alkaline salicylate. About 20 per cent. is destroyed in the tissues (Hanzlik), and the remainder is rapidly eliminated in various excretions, but chiefly in the urine. It has been assumed that the drug

leaves the body partly free and partly in combination with glycocoll, as salicyluric acid, but recent studies of Hanzlik indicate that it is excreted very largely unchanged. The excretion is attended by a slight increase in the flow of urine. Large doses not rarely cause irritation of the kidneys, as shown by the occurrence of albuminuria and cylindruria. The greenish discoloration of the urine sometimes observed after large doses of salicylates is probably due to the presence of oxidation products.

Therapeutics.—Locally, salicylic acid is a useful remedy in certain conditions of the skin. Combined with boric acid and some inert substance, such as talc or zinc oxid, and used as a dusting-powder in the stockings, it often affords relief in *hyperidrosis of the feet*.

℞. Pulveris acidi salicylici..... ℥iij (12.0 gm.)
 Pulveris acidi borici..... ℥iv (15.0 gm.)
 Pulveris talci..... ℥iv (125.0 gm.).—M.

Ointments or pastes containing from 20 to 40 grains (1.3–2.6 gm.) to the ounce (30.0 gm.) are of service in many cases of *subacute* and *chronic eczema with moderate or pronounced epidermal thickening*. Dissolved in collodion, a dram (4.0 gm.) to the ounce (30.0 mls), it is employed successfully in removing *corns* and *small warts*.

Owing to its irritant properties and its slight solubility in water, salicylic acid itself is rarely used internally, preference being given to its salts or to certain salicyl derivatives. The chief use of these compounds is in *acute rheumatism*, on which disease they seem to exert almost a specific influence, mitigating the pain, lowering the temperature, and shortening the duration of the attack, although not lessening the liability to cardiac complications. From 10 to 20 grains (0.6–1.3 gm.) of sodium salicylate, with an equal amount of sodium bicarbonate, potassium bicarbonate, or other alkaline salt, should be given every two or three hours until signs of salicylism develop or until the articular symptoms are favorably affected, when the interval between the doses should be increased.

℞. Sodii salicylatis..... ℥iv (15.0 gm.)
 Potassii bicarbonatis..... ℥iv (15.0 gm.)
 Aquæ menthæ piperitæ..... q. s. ad f ℥viiij (240.0 mls)

Sig.—A tablespoonful in water every two or three hours.

In the form of methyl salicylate or oil of wintergreen, the drug also affords some relief when applied on gauze to the affected joints. In subacute forms of the disease an ointment of the acid may be of service.

- R. Acidi salicylici..... ℥iss (6.0 gm.)
 Olei terebinthinæ..... f℥j (4.0 mls)
 Adipis lanæ hydrosi..... ℥ss (15.0 gm.)
 Adipis benzoinati..... q. s. ad ℥ij (60.0 gm.).—M.
 Sig.—Spread on muslin and keep in place by means of a flannel bandage.

In *follicular tonsillitis*, which is sometimes a precursor of rheumatism, salicylates are also efficient. They are frequently prescribed in *acute chorea* (*St. Vitus's dance*), which seems to be in some way related to rheumatism, but on the whole, the results have not been very satisfactory. In *acute gout* they are often useful, and occasionally more effective than either phenylcinchoninic acid (atophan) or colchicum. Finally, as analgesics, they are frequently helpful in *rheumatoid arthritis*, *chronic gout*, *myalgia* (stiff neck, pleurodynia, lumbago, etc.), *neuritis*, *neuralgia*, *tabetic pains* and *migraine*. The following combination of sodium salicylate with sodium bromid is sometimes effective in lessening the frequency and severity of migraine attacks:

- R. Sodii salicylatis..... ℥j (30.0 gm.)
 Sodii bromidi..... ℥iv (15.0 gm.)
 Aquæ menthæ piperitæ..... f℥vj (180.0 mls).—M.
 Sig.—A dessertspoonful in water three times a day, after meals.

A similar combination is often useful in relieving the nervous irritability and vague pains of the *menopause*.

Contraindications.—Salicyl compounds must be withheld or used with great care when there is pronounced renal irritation or active disease of the middle ear.

Administration.—Salicylates should be given after meals, preferably in some aromatic water, and well diluted. Salts prepared from oil of wintergreen ("natural salicylates") have no advantages over the much cheaper synthetic salts. Tyson, Heyn and others have shown that sodium salicylate may be given with advantage by the rectum when the stomach is intolerant. From 90 to 150 grains (6.0–10.0), in 150 to 200 mls of starch water, may be injected twice daily, after the rectum has been cleansed with a soapsuds enema.

Conner has employed it by intravenous injection, using a small needle, to avoid thrombosis, and injecting 15 to 30 grains (1.0–2.0 gm.) every 8 to 12 hours. The effect is said to have been entirely satisfactory.

SODII SALICYLAS, U. S. P.

(Sodium Salicylate, $\text{NaC}_7\text{H}_5\text{O}_3$)

Sodium salicylate is a white crystalline or amorphous powder, odorless, and of a sweetish, saline taste. It is soluble in 0.9 part

of water or in 9 parts of alcohol. The dose is from 5 to 20 grains (0.3–1.3 gm.).

Therapeutics.—It is the most commonly used of all the salts of salicylic acid. Its action is the same as that of the acid, but it has advantages in being more soluble in water and less irritant to the stomach. Like all salicylic compounds, however, it should be given after meals, well diluted.

AMMONII SALICYLAS, U. S. P.

(Ammonium Salicylate, $\text{NH}_4\text{C}_7\text{H}_5\text{O}_3$)

Ammonium salicylate occurs in clear, colorless prisms or as a white crystalline powder, freely soluble in water or in alcohol. Wood recommends it as being more agreeable to the taste and less depressing and less nauseating than the sodium salt. The dose is from 5 to 20 grains (0.3–1.3 gm.).

STRONTII SALICYLAS, U. S. P.

(Strontium Salicylate, $\text{Sr}(\text{C}_7\text{H}_5\text{O}_3)_2$)

Strontium salicylate occurs as a white, crystalline powder, of somewhat sweet saline taste. It is soluble in 19 parts of water. The dose is from 5 to 20 grains (0.3–1.3 gm.).

Strontium salicylate is sometimes better borne than sodium salicylate, but its action is similar.

METHYLIS SALICYLAS, U. S. P.

(Methyl Salicylate, Oil of Wintergreen, $\text{CH}_3\text{C}_7\text{H}_5\text{O}_3$)

Methyl salicylate is produced synthetically by distilling methyl alcohol with salicylic and sulphuric acids, or by distilling *Gaultheria procumbens* (wintergreen or teaberry) or *Betula lenta* (sweet birch). It is a colorless, yellowish, or reddish liquid, having the characteristic odor and taste of wintergreen. It is equivalent to the natural oil of wintergreen and the oil of sweet birch, which consist almost entirely of methyl salicylate. The dose is from 5 to 20 minims (0.3–1.2 mls.).

Therapeutics.—Methyl salicylate may be used internally in *rheumatism* instead of sodium salicylate or other inorganic salicylates, although it is much more prone to disturb digestion than the latter, and its strong odor and taste often turn the patient against it. Externally, it serves an excellent purpose as a local application for the affected joints. For internal use methyl salicylate may be given in capsules, in emulsion, or on sugar. The synthetic preparation is as efficient as the natural oil of wintergreen, and very much cheaper.

Mesotan.—This is the trade name of the salicyl ester of methyloxymethyl. It is a yellow liquid, miscible with oils and other organic solvents. Diluted with from 20 to 30 per cent. of some bland oil, it has been recommended as a local remedy in rheumatic affections. Though more irritating, it does not appear to be any more effective than methyl salicylate. Moreover, it is costly.

BISMUTHI SUBSALICYLAS, U. S. P.

(Bismuth Subsaliolate, $\text{Bi}(\text{C}_7\text{H}_5\text{O}_3)_3\text{Bi}_2\text{O}_3$)

Bismuth subsaliolate is a white, amorphous or crystalline powder, odorless and tasteless, and insoluble in water. It is sometimes used as an intestinal antiseptic and astringent in *diarrhea*. The dose is from 5 to 15 grains (0.3–1.0 gm.).

PHENYLIS SALICYLAS, U. S. P.

(Phenyl Salicylate, Salol, $\text{C}_6\text{H}_4.\text{OH}.\text{CO}_2(\text{C}_6\text{H}_5)$)

Salol is a white crystalline powder, of a faintly aromatic odor and taste. It is almost insoluble in water, but is soluble in 6 parts of alcohol. It represents salicylic acid ($\text{C}_6\text{H}_4.\text{OH}.\text{COOH}$) with the H of the carboxyl (COOH) group replaced by phenyl (C_6H_5). The dose is from 3 to 10 grains (0.2–0.6 gm.).

Pharmacologic Action and Therapeutics.—Salol resists to a great extent the action of the gastric juice, but is slowly decomposed by the alkaline secretion of the intestine into salicylic acid (60 parts) and phenol (40 parts). These components are rapidly absorbed. After very large doses poisoning results from the phenol rather than the salicylic acid.

Salol is sometimes used in *rheumatism*, but it is inferior to sodium salicylate, owing to the relatively low percentage of salicyl and the toxicity of the phenol component. It may be employed successfully, however, as an analgesic in the milder forms of *arthritis* and in *myalgia*. As its dissociation does not occur until it leaves the stomach, it may sometimes be employed advantageously as an intestinal antiseptic in *enteritis* and other conditions associated with excessive putrefaction. Combined with copaiba or oil of sandalwood, it may be of service as a urinary antiseptic in *cystitis*, *urethritis*, etc. It should be used with considerable caution when there are evidences of active nephritis. Salol and keratin (the alkali-soluble component of horn) are the substances usually employed for coating pills and capsules which are intended to pass through the stomach unchanged and to liberate their contents in the intestine. Tablets or hard pills of salol may fail of decomposition in the intestine and be discharged in the feces

unchanged or may even give rise to intestinal calculi. Leo, Robin and Treves have each found concretions of salol in the feces.

ACIDUM ACETYLSALICYLICUM

(Acetylsalicylic acid, Aspirin, $C_6H_4.O(COCH_3).COOH$)

Acetylsalicylic acid, or aspirin, differ from salol in being an acyl instead of a phenyl derivative of salicylic acid. The H of the OH group in salicylic acid ($C_6H_4.OH.COOH$) is replaced by acyl ($COCH_3$). It is a white, crystalline odorless powder of sour taste. It is slightly soluble in water, but readily soluble in alcohol. It is incompatible with alkalis. The dose is from 5 to 15 grains (0.3–1.0 gm.) in capsules, powders or tablets.

Pharmacologic Action and Therapeutics.—Acetylsalicylic acid is said to pass unchanged through the stomach and in the presence of the alkaline secretions of the intestine to yield sodium salicylate and sodium acetate. It is less irritant to the stomach and less toxic than sodium salicylate, but also less powerful as an analgesic, antipyretic and antirheumatic. Although not usually followed by unpleasant effects, large doses, and even small doses in susceptible persons, occasionally produce gastric disturbances, giddiness, temporary deafness, localized or general edema, urticaria, or collapse.

The action of acetylsalicylic acid is too weak to be relied upon in acute rheumatism, but the drug is efficacious as an analgesic in "colds," sore throat, influenza, headache, neuralgia, neuritis, myalgia and the milder forms of arthritis. In catarrhal infections of the upper respiratory tract, such a combination as the following is often useful when given in conjunction with large doses of the solution of potassium citrate, but it should not be continued for more than a day or two:

℞. Pulveris ipecacuanhæ et opii. gr. xl (2.5 gm.)
 Acetphenetidini. gr. xl (2.5 gm.)
 Acidi acetylsalicylici. ʒj (4.0 gm.).—M.
 Fiant chartulæ No. xii.
 SIG.—One powder every three or four hours.

Salophen (*Acetyl-paramido-phenyl Salicylate*).—This salicyl ester of acetparamidophenol occurs in tasteless and inodorous white scales, insoluble in water, but soluble in alcohol or ether. It contains about 50 per cent. of salicylic acid. It was introduced as a substitute for salol, on account of the ill effects thought to result from the liberation of phenol from the latter. It is decomposed in the intestine into salicylic acid and the comparatively innocuous acetyl-paramido-phenyl. It is much less effective in

rheumatism than sodium salicylate, but being tasteless and comparatively unirritating to the stomach, it may sometimes be used with advantage as an analgesic in "colds," *sore throat*, *neuralgia*, *myalgia*, etc. The dose is from 5 to 15 grains (0.3–1.0 gm.).

SALICINUM, U. S. P.

(Salicin, $C_{13}H_{18}O_7$)

Salicin is a glucoside obtained from several species of willow (*salix*) and poplar (*populus*). It occurs in white, silky needles or as a crystalline powder, odorless, and of a very bitter taste. It is soluble in 23.5 parts of water or in 88.5 of alcohol. The dose is from 10 to 30 grains (0.6–2.0 gm.). Salicin was the first of the salicylic preparations to be used in rheumatism, MacLagen, of Dundee, having prescribed it in 1874, a year before the introduction of salicylic acid by Buss, of Basle. It is partially converted in the body into salicylic acid, and rapidly appears in the urine partly as salicin and partly as saligenin, salicyluric acid, and salicylic acid. It is well borne by the stomach, but it is far less active and reliable than salicylic acid or the salicylates.

ACIDUM PHENYLCINCHONINICUM, U. S. P.

(Phenylcinchoninic Acid, Cinchophen, Atophan, $C_6H_5.C_9H_8N.COOH$)

Phenylcinchoninic acid is derived from quinolin by the substitution of phenyl (C_6H_5) for one H and carboxyl ($COOH$) for another H. Quinolin (C_9H_7N) is naphthalin ($C_{10}H_8$) with a CH group replaced by N. Phenylcinchoninic acid occurs in small colorless needles or as a white or yellowish-white crystalline powder, odorless and of a bitter taste. It is insoluble in cold water and only slightly soluble in cold alcohol. The dose is from 5 to 15 grains (0.3–1.0 gm.), in powders, capsules or tablets, three or four times a day. It should be taken with large draughts of water.

Pharmacologic Action and Therapeutics.—Cinchophen has an action similar to that of salicylic acid and the salicylates. It is antipyretic, analgesic and antirheumatic, and possesses even to a greater degree than salicylic acid the power to cause an increased elimination of uric acid from the blood. The increase of uric acid in the urine is apparently brought about by a lowering of the threshold of the kidneys for this substance and lasts until the administration of the drug is discontinued or until the concentration of uric acid in the blood reaches an irreducible minimum. When the uric acid concentration of the blood is high, precipitation may occur in the urine before it is passed.

Phenylcinchoninic acid does not change the non-protein nitrogen content of the blood (Denis) and when the kidneys are diseased it does not reduce the concentration of uric acid (Fine and Chace). Its effect on gouty tophi is doubtful.

Phenylcinchoninic acid has been used with considerable success in the acute and subacute manifestations of *gout*. In *chronic gout* it is much less effective. In *rheumatism* and other painful conditions of the joints it is usually inferior to sodium salicylate and acetylsalicylic acid. It does not often produce untoward effects, but occasionally it causes vertigo, digestive disturbances, or a cutaneous eruption of an urticarial, erythematous or purpuric character. Uric acid calculus disease contraindicates its use, because of the likelihood of uric acid precipitation within the urinary tract.

Neocinchophen (Tolysin, Novatophan).—This compound is an ethyl-methyl ester of cinchophen. It is used in the same doses and for the same purposes as cinchophen, but it has an advantage over the latter in being virtually tasteless.

ACIDUM BENZOICUM, U. S. P.

(Benzoic Acid, $C_6H_5.COOH$)

Benzoic acid (see p. 291) is a derivative of benzol (C_6H_6), an H atom of the latter being replaced by the carboxyl ($COOH$) group. It may be obtained from benzoin (see p. 290) or from the urine of herbivorous animals, or may be produced synthetically from toluol ($C_6H_5CH_3$), a coal-tar derivative. It occurs in white or yellowish lustrous scales or friable needles having an aromatic odor and a pungent taste. It is sparingly soluble in water, but freely soluble in alcohol, ether or oils. The dose is from 5 to 15 grains (0.3–1.0 gm.).

Therapeutics.—The pharmacologic action of benzoic acid resembles that of salicylic acid. Compared with the latter, it has about equal germicidal power, but it is much less efficient as an analgesic and antirheumatic. Internally, it is sometimes useful as a urinary antiseptic in *cystitis with ammoniacal urine*; and externally, in the form of balsam of Peru (see p. 292), it is of service as a parasiticide in *scabies*.

NAPHTHALENUM

(Naphthalen, Naphthalin, Tar Camphor, $C_{10}H_8$)

Naphthalen is a hydrocarbon obtained by distilling coal-tar between 180° – 250° C. (356° – 482° F.). It occurs in white, shining scales, having a strong odor of coal-tar and a burning

taste. It is insoluble in water, soluble in 13 parts of alcohol, and in all proportions in ether or chloroform. The dose is from 2 to 8 grains (0.13–0.5 gm.).

Therapeutics.—Naphthalen is an effective insecticide against moth and lice. For lice a mixture consisting of naphthalen 96 per cent., creosote, 2 per cent., and magnesium silicate, 2 per cent. has been especially recommended (Kinloch). Internally, it was at one time used as an intestinal antiseptic in *diarrhea*, but it has been completely displaced by betanaphthol.

BETANAPHTHOL, U. S. P.

(Betanaphthol, Naphthol, $C_{10}H_7OH$)

Betanaphthol is a phenol derivative from coal-tar, and prepared by introducing an OH group into naphthalen. It occurs in white, shining scales or as a yellowish-white crystalline powder, having a faint, phenol-like odor and a pungent taste. It is soluble in about 1000 parts of water, and freely soluble in alcohol or ether. The dose is from 2 to 10 grains (0.13–0.6 gm.).

Pharmacologic Action and Therapeutics.—Betanaphthol resembles phenol in its action, but it is less poisonous. Large doses, however, not infrequently give rise to considerable irritation of the kidneys and bladder and to inflammatory changes in the retina. Locally, in concentrated form, it is irritating to mucous membranes and raw surfaces. Absorption readily follows its local application. Its germicidal power is greater than that of phenol.

Internally, betanaphthol is sometimes useful as an antiseptic in *chronic diseases of the stomach* and in *diarrhea*. In doses of 15 grains (1.0 gm.), repeated in two hours, it has been used in *uncinariasis* or *hook-worm disease*, but it is less efficient than oil of chenopodium or thymol and more likely to cause poisoning. It is best administered in capsules.

Externally, it is efficacious as a parasiticide and stimulant application in certain diseases of the skin. In *scabies* and in *ringworm of the scalp or body* it may be employed as an ointment in the strength of a dram (4.0 gm.) to the ounce (30.0 gm.). Ointments containing from $\frac{1}{2}$ to 1 dram (2.0–4.0 gm.) to the ounce (30.0 gm.) have been used also with some benefit in *psoriasis*, but, as a rule, the drug is less useful in this disease than either chrysarobin or tar.

Benzonaphthol.—This compound is prepared by acting on betanaphthol with benzoyl chlorid. It is said to escape the action of the gastric juice, and to be split up into its components

in the intestine. In doses of from 5 to 10 grains (0.3–0.6 gm.), it is a good intestinal antiseptic, having at least one advantage over betanaphthol in being tasteless.

Bismuthi Betanaphtholas, U. S. P. (Bismuth Betanaphthol, Orphol).—This preparation is a combination of bismuth oxid and betanaphthol. It is a light-brown, insoluble powder, odorless and tasteless. As its decomposition is mainly effected after it leaves the stomach, it may be useful as an antiseptic and astringent in the various forms of intestinal catarrh. The dose is from 10 to 30 grains (0.6–2.0 gm.).

ACRIFLAVIN AND PROFLAVIN

($C_{14}H_{14}N_3Cl \cdot H_2O$ and $C_{13}H_{11}N_3H_2SO_4 \cdot H_2O$)

Acriflavin and proflavin are dyes derived from acradin, a base found in coal-tar. They occur as brownish-red crystalline powders, which are readily soluble in water or alcohol. They are claimed to have a strong antiseptic power, which is enhanced rather than impaired by the presence of blood-serum, and to be free from irritant and toxic properties. Acriflavin is said to be the more powerful antiseptic of the two, but to be less rapid in action. A solution of 1:1000 in normal salt solution is well spoken of for cleansing *wounds* and for wet-dressings. As the antiseptic action is persistent, frequent change of dressings is unnecessary. According to Crile, it is not suitable for long continued use. Acriflavin and proflavin are also effective in *gonorrhea*, a solution of 1:1000 in normal salt solution being used for injections and a solution of 1:4000 for irrigations.

CHLORUM

(Chlorin, Cl)

Chlorin is a heavy, yellowish-green gas, of a suffocating odor and a caustic taste. It may be prepared by heating together sodium chlorid, sulphuric acid, and manganese dioxid or by acting upon chlorinated lime with an acid.

In concentrated form chlorin acts as a powerful irritant, even upon cutaneous surfaces. When inhaled it excites pain in the chest, cough, dyspnea, spasm of the vocal cords, and, ultimately, mucopurulent or fibrinous bronchitis with inflammation and edema of the lungs. Owing to its affinity for hydrogen and its power to separate nascent oxygen from water, it is an energetic germicide, especially in the presence of moisture. For the same

reasons it is also an active deodorizer. As a gaseous disinfectant for rooms, it has serious disadvantages in being exceedingly irritant and poisonous, in being destructive to wall-paper and other colored fabrics, and in being so heavy that it diffuses with difficulty. For disinfectant purposes it is employed chiefly in the form of chlorinated lime or chlorinated soda.

CALX CHLORINATA, U. S. P.

(Chlorinated Lime, Bleaching Powder)

Chlorinated lime is a preparation containing not less than 30 per cent. of available chlorin, and is obtained by acting on slaked lime with chlorin gas. It consists chiefly of the hypochlorite and the chlorid of calcium, and appears as a grayish-white powder, having a strong odor of chlorin and a disagreeable saline taste. It is partially soluble in water and in alcohol.

Action and Uses.—A solution of 0.5 to 1 per cent. of freshly prepared chlorinated lime kills most bacteria within ten minutes. A 0.5 per cent. solution makes a reliable disinfectant wash for *bare walls* and *woodwork*. A solution of the same strength is also useful for disinfecting *white clothes*. A 3 per cent. solution may be employed to sterilize *feces*, *sputa*, and other excreta. Only fresh preparations or those that have been preserved in air-tight containers should be used, as the compound readily parts with its chlorine and loses strength on exposure to air and moisture. According to Dakin, the germicidal power of both a hypochlorite and free hypochlorous acid depend not so much on the liberation of nascent oxygen, as on the replacement of hydrogen in the NH group of organic compounds by chlorin, with the formation of substances known as chloramins.

In many municipalities chlorinated lime is used alone or in conjunction with alum coagulation and sedimentation or slow sand filtration as a means of purifying the public water supply. The advantages of the method are its cheapness, harmlessness, simplicity, and efficiency. The amount of powder employed ranges from 5 to 15 pounds for each million gallons of water. An objection to the hypochlorite treatment of water is the liability to the production of an unpleasant taste or odor, especially in cold weather, due not so much to the hypochlorite itself, as to compounds which it forms with certain organic matters sometimes present in the water. In some cities liquefied chlorine gas produced by the electrolysis of brine is substituted for chlorinated lime.

Bleaching powder is also useful for the disinfection of swimming pools, slaughter-houses, bake-houses, dairies, cellars, etc.

LIQUOR SODÆ CHLORINATÆ, U. S. P.

(Solution of Chlorinated Soda, Labarraque's Solution)

The official solution of chlorinated soda is an aqueous solution of chlorin compounds containing not less than 2.5 per cent. of available chlorin. It is a clear, pale greenish liquid, having a faint odor of chlorin and a disagreeable alkaline taste. *Javelle water* (eau de Javelle) is a similar preparation of chlorinated potash.

Owing to its alkaline reaction, it is too irritant to be used as a germicide for surgical purposes. A solution of sodium hypochlorite prepared by a process devised by Dakin (surgical solution of chlorinated soda), however, has a neutral reaction, is non-toxic, and is virtually non-irritant to wounds, although it is somewhat irritant to the skin and is decidedly irritant to the peritoneum. It has a solvent action on necrotic tissue and silk ligatures, and has some tendency to loosen catgut sutures.

Dakin's solution has been used with great success for the *irrigation of infected wounds, abscess cavities, empyemata*, etc., and as a *wash for the nose and throat in infectious diseases*. To be effective, the solution should not contain less than 0.45 per cent. of sodium hypochlorite, and to be free from irritant properties not more than 0.5 per cent. of the hypochlorite. The best results have been secured by Carrel and other surgeons with the following modification of Dakin's original formula.*

1. Chlorinated lime (bleaching powder)..... 200 gm.
Sodium carbonate, dry..... 100 gm.
Sodium bicarbonate..... 80 gm.

2. Put the chlorinated lime in a 12-liter flask with 5 liters of ordinary water, and let it stand over night.

3. Dissolve the sodium carbonate and bicarbonate in 5 liters of cold water.

4. Pour (3) into the flask containing (2), shake it vigorously for a minute, and let it stand to permit the calcium carbonate to settle.

5. After half an hour siphon off the clear liquid and filter it through paper to obtain a perfectly limpid product. This must be kept protected from the light.

The antiseptic solution is then ready for surgical use; it contains about 0.5 gm. per cent. of sodium hypochlorite with small amounts of neutral soda salts; it is practically isotonic with blood-serum. It should meet the following tests:

Test.—Put about 20 mls of the solution in a glass and pour on its surface a few centigrams of phenolphthalein in *powder*; shake it with a circular movement, as in rinsing; the liquid should remain colorless. A more or less marked red discoloration indicates the presence of a notable quantity of free alkali, or incomplete carbonation, imputable to an error in technic.

* Lewis A. Stimson; Jour. Amer. Med. Assoc., Dec. 2, 1916.

Errors to be Avoided.—Never heat the solution. If in an emergency it is necessary to triturate the chlorinated lime in a mortar, do so only with water, never with the solution of the soda salts.

Titration.—To 10 mls of the solution add 10 mls of distilled water, 2 gm. of potassium iodid and 2 mls of acetic acid. Pour into this mixture a decinormal (2.48 per cent.) solution of sodium thiosulphate (hyposulphite) until it is decolorized. The number of mls of thiosulphate solution employed multiplied by 0.03725 equals the percentage of sodium hypochlorite in the solution.

Hypochlorites should not be used in conjunction with other antiseptics, nor with alcohol or ether. Wounds which have been previously treated with iodine may take on a dark color, due to reliberation of iodine, but this is of no importance. Sound skin around wounds should be protected from the irritant action of the solution by petrolatum.

Hychlorite.—This is a solution of chlorinated soda, having the properties and uses of the official solution, but containing a larger percentage of available chlorine and a less degree of alkalinity. For direct application to mucous membranes it may be used in full strength or diluted with 1 or 2 parts of water; for simple irrigation of wounds and cavities it is used in dilutions of 1:1000 to 1:100; for continuous irrigation of infected wounds, as in the Carrel technic, it should be diluted with 7 volumes of water. In order that due allowance may be made for decrease in available chlorine, which is at the rate of 12 per cent. per year, the date of bottling is stamped on each bottle.

Antiformin.—This is a strongly alkaline solution of sodium hypochlorite, each 100 mls containing 5.68 grams of available chlorine, 7.8 grams of sodium hydroxid, and 0.32 grams of sodium carbonate. It has been recommended for general purposes of disinfection (5 per cent. solutions), but it is chiefly useful for the demonstration of tubercle bacilli (15 per cent. solution) in sputum, feces, etc., as it dissolves organic matter and all bacteria, except those that are acid-fast.

CHLORAMINS

According to Dakin, the germicidal power of the hypochlorites results from their reaction with proteins and the formation of compounds known as chloramins. Two of the latter have been prepared synthetically: chloramin-T and dichloramin-T.

Chloramin-T (Chlorazene).—This compound, which is sodium paratoluene sulphochloramid, is a white, crystalline powder, with a slight odor of chlorine. It has properties similar to those of Dakin's solution of chlorinated soda, but it may be employed more conveniently, is more stable, more actively germicidal, and

even less irritant. On the other hand, it has no solvent action on necrotic tissue. It is decomposed by oils.

Chloramin-T may be used in from 1 to 2 per cent. solutions for the same purposes as the surgical solution of chlorinated soda. Its chief drawback is that it disappears rapidly from the wound exudate and the solution must be renewed every 2 hours. To overcome this objection Dakin introduced under the name of dichloramin-T, paratoluene-sulphondichloramid.

Dichloramin-T.—This is a yellowish crystalline powder only sparingly soluble in water, but soluble in chlorinated oils. A solution in chlorinated paraffin is known as *chlorcosane*. Chlorinated oils are used as solvents so that the oil will not abstract the chlorine from the compound. The solution is more germicidal than that of chloramin-T and the effect is produced more gradually and is more sustained. It is inferior to Dakin's solution of chlorinated soda in being somewhat more irritant, especially to granulating wounds, and in having less solvent action on necrotic tissue, but it has an advantage in not loosening catgut and so favoring secondary hemorrhage. Solutions of from 1 to 10 per cent. have been used with considerable success in *infected wounds* and *burns*. They should be applied by a glass syringe or medicine dropper, as metal decomposes them. The solutions are more or less unstable and should not be kept more than a few days.

BRILLIANT GREEN

Brilliant green, diamino-triphenylmethane, is an effective germicide, although it soon loses its power in the presence of serum, and therefore must be frequently renewed. It is virtually non-irritant and non-toxic. Dissolved in normal saline solution in the strength of 1 to 1000, it may be applied to wounds, both as a lotion and on gauze.

IODUM, U. S. P.

(Iodin, I)

Therapeutics.—A 3 to 5 per cent. alcoholic solution of iodine is a valuable antiseptic both for cleansing the skin before operations and for the treatment of wounds. As a disinfectant for the skin it may be applied two hours before operation and again when the patient is on the table. When iodine is to be used, the skin should not be scrubbed or wet shaved within several hours of the operation, as moisture tends to swell the epithelial surface and to prevent the entrance of the antiseptic into the follicles. If the abdomen is to be opened and iodine has been applied to the field of operation, the skin should be wiped with alcohol before

the incision is made and every precaution should be taken to prevent the intra-abdominal structures from coming in contact with the iodized surface, otherwise severe irritation of the peritoneum, with consequent formation of adhesions, is very likely to occur. Dirty wounds may be cleansed with tincture of iodine and large cavities may be irrigated with a solution of 1 fluidram (4 mls) of the tincture of iodine in 1 quart (1000 mls) of water.

IODOFORMUM, U. S. P.

(Iodoform, CHI_3)

Iodoform, or triiodo-methane, is methyl with three atoms of H replaced by three of iodine. It is made by heating in a closed vessel iodine, alcohol, sodium hydroxide and water. It occurs as a fine, lemon-yellow powder or in lustrous crystals having a peculiar penetrating odor and a sweetish, iodine-like taste. It is nearly insoluble in water, soluble in 60 parts of alcohol, and readily soluble in ether or chloroform. Iodoform contains about 97 per cent. of iodine. The dose is from 1 to 5 grains (0.06–0.3 gm.).

PREPARATION

Unguentum Iodoformi, U. S. P. (10 per cent. in benzoated lard)

Pharmacologic Action.—Upon mucous membranes and raw surfaces iodoform acts as an antiseptic and mild analgesic. It is readily absorbed from wounds, sinuses, etc., entering the blood partly as iodine, which it liberates in the presence of the body fluids, partly as organic compounds of iodine, and partly, it is believed, as iodoform. Soon after absorption, iodine appears in the various secretions; elimination, however, is mainly effected by the kidneys, which slowly excrete the drug in the form of iodides, iodates, and organic compounds, but not as iodoform. When absorbed too freely it induces an intoxication which may prove fatal. The symptoms of iodoform-poisoning resemble somewhat those of cerebral meningitis, and include lassitude, headache, mental depression, nausea and vomiting, hallucinations, coma, and collapse. In some cases there has been, in addition, high fever, and in others, a diffuse erythematous or vesicular rash. Postmortem examination reveals fatty changes in the viscera and sometimes congestion of the meninges. As neither iodine nor iodides in overdoses cause cerebral symptoms, it is possible that the latter may be due to the action of iodoform itself. The majority of cases of poisoning have occurred in old persons.

Although the favorable action of iodoform in certain types of infected wounds is generally conceded, the manner of its operation is still somewhat obscure. The drug itself is virtually without germicidal power, but when in contact with the tissues it retards germ growth partly by liberating iodine and partly, it is supposed, by inhibiting serous exudation and by stimulating phagocytosis.

In some persons local applications of iodoform prove irritating and cause eczematous or pustular eruptions.

Treatment of Poisoning.—The indications are to suspend applications, to sustain the strength of the patient, and to favor elimination by subcutaneous injections of normal saline solution and the administration of alkaline diuretics. Sodium bicarbonate has been recommended as an antidote.

Therapeutics.—Iodoform is especially useful as a local application in *suppurating or putrid wounds* and in *syphilitic, chancroidal, and tuberculous processes*. In the form of iodoform gauze it is frequently used as a packing for *deep wounds, sinuses, fistulae, and the rectal, vaginal and nasal cavities*. *Cold abscesses and tuberculous joints* are often successfully treated by injecting into them, once a week, iodoform (5 to 10 per cent.) in sterile olive oil or glycerin, to the amount of $\frac{1}{2}$ to 3 fluidounces (15.0–90.0 mls). The iodoform should first be sterilized by soaking it for several days in a solution of 1:1000 corrosive sublimate and then thoroughly washing it in sterilized water.

As a local analgesic, iodoform is useful in relieving the pain and dysphagia of *tuberculous laryngitis*. It is best applied by insufflation. Suppositories of the drug (3 gr.—0.2 gm.) are also of service in *painful hemorrhoids and fissure of the anus*.

Iodoform has been used to some extent as an internal remedy in *pulmonary tuberculosis*, but the results have not been encouraging. While many agents have been recommended for disguising the disagreeable odor of iodoform, none has proved very successful; the best, however, are the volatile oils, such as bergamot anise, and cumarin, the odorous principle of Tonka bean.

IODOL

(Tetra-iodo-pyrrol, C_4I_4NH)

Iodol is prepared by acting upon pyrrol, a principle obtained from bone oil, with iodine. It contains a little less than 90 per cent. of iodine, and appears as a yellowish, crystalline powder, free from odor and taste. It is almost insoluble in water, but it is freely soluble in alcohol, ether, or oils.

As an antiseptic dusting-powder it is inferior to iodoform, although it has an advantage in being odorless.

THYMOLIS IODIDUM, U. S. P.

(Thymol Iodid, Di-thymol-di-iodid, Aristol, $C_{20}H_{24}O_2I_2$)

Thymol iodid, or aristol, is obtained by acting upon thymol in alkaline solution with iodine dissolved in potassium iodid. It contains about 45 per cent. of iodine, and appears as a brownish-red powder, tasteless and almost odorless. It is readily soluble in ether or oils, but it is insoluble in water. It is decomposed by heat, light, acids, alkalis, alcohol, and corrosive sublimate.

It is employed as a substitute for iodoform. While it has advantages in being odorless and less toxic than iodoform, it is more unstable, more costly, and less effective. It may be applied pure or dissolved in ether or oil.

EUROPHEN

(Di-isobutyl-ortho-cresol-iodid, $C_{22}H_{29}O_2I$)

EuropHEN is obtained by precipitating an alkaline solution of isobutyl-ortho-cresol with a solution of iodine in potassium iodid. It contains 28 per cent. of iodine, and appears as a very bulky, yellow, amorphous powder, of an aromatic odor. It is insoluble in water or glycerin, but freely soluble in alcohol, ether, or oils. It is a fairly good substitute for iodoform, but on the whole it is less efficient.

NOSOPHEN

(Tetra-iodo-phenol-phthalein, $(C_6H_2I_2OH)_2C_8H_4O_2$)

Nosophen is obtained by the action of iodine on a solution of phenolphthalein. It is a pale yellow, inodorous, and tasteless powder. It contains 60 per cent. of iodine. With bases it forms salts, the most important of which is the sodium salt (*antinosin*). It differs from iodoform in being an active antiseptic and in not yielding its iodine to the tissues.

FORMALDEHYDUM

(Formaldehyd, Oxymethylene, $HCHO$)

Formaldehyd is a colorless and irritant gas obtained by oxidizing methyl alcohol (CH_3OH). A 37 per cent. aqueous solution of the gas is official as *Liquor Formaldehydi*. The latter contains a variable amount of free methyl alcohol to prevent polymerization. It is a clear, colorless liquid, having a very pungent odor and a caustic taste. Other preparations of the same composition are known as *formalin*, *formal*, etc.

In pure aqueous solution the gas readily polymerizes forming *paraformaldehyd*, *paraform*, or *trioxymethylene* (HCHO)₃, which is official as *Paraformaldehydum*. The latter occurs in white, friable masses or as a powder, having a slight odor of formaldehyd. It is slowly soluble in water, is insoluble in alcohol, and on heating yields formaldehyd.

Pharmacologic Action.—Formaldehyd is an intensely irritating gas, causing, when inhaled in concentrated form, severe inflammation of the mucous membrane of the entire respiratory tract. On cutaneous surfaces concentrated solutions, or even dilute solutions if the contact be prolonged, not infrequently excite an erythematous or eczematous eruption. Taken by the mouth in strong concentrations or large doses, it causes acute gastritis. It reacts with proteins forming more or less stable compounds, but when added to shed blood in the proportion of 1 to 200 it retards coagulation. In the presence of moisture it is an active antiseptic or a germicide, according to the concentration in which it is used. A dilution of 1:20,000 inhibits the growth of typhoid bacilli and a dilution of 1:1000 kills anthrax bacilli and their spores in one hour. Concentrations higher than 1:10,000 diminish the digestibility of proteins and have a weak inhibiting effect on digestive enzymes.

Formaldehyd is rapidly absorbed from the digestive tract and the lungs, and after absorption it is relatively non-toxic. In the tissues it is largely oxidized to formic acid, a part of which is also finally destroyed. A small part of the formaldehyd may be converted into hexamethylenamin. The part of the drug which escapes complete destruction in the body is excreted chiefly by the kidneys as formic acid. Formaldehyd itself, however, may be eliminated by the kidneys, lungs and digestive tract after the administration of large doses intravenously.

Toxicology.—The symptoms of formaldehyd-poisoning consist of severe abdominal pain, vomiting, dyspnea, unconsciousness and collapse. If the patient survives, evidences of intense renal irritation, such as hematuria, albuminuria, or even persistent anuria, may supervene. Death may occur within 24 hours, but in non-fatal cases recovery is usually rapid. Doses of 60 or 70 mils have been survived.

Treatment.—This consists in administering dilute ammonia or ammonium salts, which form with formaldehyd the comparatively non-toxic hexamethylenamin, in washing out the stomach, in giving demulcent drinks, and in combating collapse with stimulants and hot applications.

Therapeutics.—Formaldehyd has been extensively employed as a *disinfectant for rooms*. It is, however, scarcely more than a

surface disinfectant, for while it is very diffusible it has little penetrating power. It unites readily with hydrogen sulphid, mercaptan, ammonia and fetid ammonia bases to form inodorous compounds, and therefore is an efficient *deodorizer*.

As a room disinfectant, it has advantages in being comparatively harmless to higher forms of animal life and in having no injurious effects on colored fabrics. Owing to its weak penetrating power, it is not a reliable disinfectant for upholstered furniture, carpets, bedding, books, etc. (see p. 387). As the aqueous solution when vaporized from an open vessel loses much of its germicidal power through the polymerization of the formaldehyd into paraform, some special device has been found necessary for securing an adequate supply of the gas. Lamps devised for generating formaldehyd directly from methyl alcohol were first employed, but they did not prove reliable. A sufficient quantity of gas may be obtained by vaporizing paraform tablets in a suitable lamp, or by subjecting a fine stream of the aqueous solution by means of a special contrivance to a high degree of heat. At least 60 paraform tablets or a quart (1.0 L.) of the official solution of formaldehyd should be vaporized for every 1000 cubic feet of room to be disinfected. Another simple but very reliable method is to add the solution of formaldehyd to powdered potassium permanganate. The mixture should be made in a large galvanized iron or tin pail placed on bricks in a wash tub containing water, and 20 ounces (600 mls) of liquor formaldehydi and $8\frac{1}{2}$ ounces (245.0 gm.) of the permanganate should be used for every 1000 cubic feet of room space requiring disinfection. A cheaper method consists in substituting 3 pounds (1.5 kg.) of fresh unslaked lime in small fragments for the potassium permanganate and pouring over it a solution of aluminum sulphate and formaldehyd, which is made by dissolving 4 ounces (125.0 gm.) of aluminum sulphate in one-half pint (240.0 mls) of hot water, allowing the solution to stand for a few hours and then adding 1 pint (475.0 mls) of liquor formaldehydi. To secure the best results with any of these methods the room should be sealed before the operation, and should be kept closed for at least 8 hours. Subsequently, ammonia water may be sprayed in the room to destroy the odor of the formaldehyd.

Formaldehyd, even in weak solutions, is so irritant to raw surfaces that it is not suitable for wound treatment. A one-half per cent. solution (12.5 mls. of liquor formaldehydi to 1 liter of water), however, is sometimes used to irrigate *sinuses*, *abscess cavities* and *suppurating joints*. Formaldehyd gas, liberated from paraform tablets by the application of heat, is

valuable for *disinfecting rubber catheters* and other *rubber articles*. Weak solutions of formaldehyd have been employed to some extent by intravenous injection in the treatment of *septicemia*, but the procedure has little to recommend it, as the injections are intensely painful and the formaldehyd in the blood is very rapidly oxidized with the formation of irritant formic acid. A lotion containing 2 per cent. of liquor formaldehydi (25.0 mls to 0.5 liter of water) is sometimes very efficacious in *bromidrosis* and *hyperidrosis*, but it should not be used if the skin is broken. A 10 per cent. solution of the official preparation in excess is a reliable disinfectant for *stools*, *sputa*, etc., but the irritating fumes prevent its use in the sick room. When added to urine as a preservative it prevents the coagulation of serum albumin by heat.

There is considerable evidence to show that formaldehyd added to milk (1:10,000) lessens its nutritive value, interferes with digestion and favors the occurrence of inflammatory changes in the alimentary canal.

Incompatibles.—Ammonia, ammonium salts, alkalis, gelatin and tannin.

Glutol.—This is a compound of formaldehyd and gelatin, appearing as a gray, odorless and tasteless powder. It has been employed to some extent as a substitute for iodoform in the treatment of *infected wounds* and *ulcers*. Glutol capsules are sometimes used as containers for drugs that are intended to pass into the bowel without action or change in the stomach, but they are not wholly reliable.

Tannoform (see p. 354) is a combination of tannin and formaldehyd. It is chiefly used as a dusting-powder in *hyperidrosis* and *bromidrosis*.

HEXAMETHYLENAMINA, U. S. P.

(Hexamethylenamin, $(\text{CH}_2)_6\text{N}_4$)

Hexamethylenamin is the product of the action of formaldehyd or ammonia. It occurs in colorless, odorless crystals or as a white crystalline powder having a slightly sweetish taste. It is soluble in 1.5 parts of water or 12.5 parts of alcohol. The dose is from 5 to 10 grains (0.3–0.6 gm.), with a liberal amount of water, four times a day. Hexamethylenamin is marketed under a variety of trade names, such as urotropin, cystogen, formin, etc.

Pharmacologic Action and Therapeutics.—Hexamethylenamin itself has neither destructive nor inhibitory influence on bacterial growth, but in the presence of free acids it liberates formaldehyd, which is an energetic germicide. The drug is

without irritant properties and when taken by the mouth is rapidly absorbed, appearing in all normal body fluids, as well as in various pathologic exudates. Under ordinary conditions, however, it yields formaldehyd in appreciable amounts only in the urine, gastric juice and sweat. It is excreted mainly in the urine, and when this secretion is highly acid so much formaldehyd may be liberated from large doses of hexamethylenamin as to cause serious irritation of the kidneys and bladder. Toxic doses give rise to abdominal pain, vomiting, diarrhea, dysuria, hematuria and albuminuria.

Hexamethylenamin is a valuable urinary antiseptic when the urine is of an acid reaction. It is especially useful in *simple bacteriuria*, *catarrhal cystitis* and *pyelitis*. When the bacteria, instead of being free in the urine, are chiefly in the tissues of the bladder, as in tuberculous and gonorrheal cystitis, the drug is of little value. If the urine is alkaline, acid sodium phosphate should be given in doses of 10 grains (0.6 gm.) or more every two hours until it becomes acid. The two drugs should not be administered at the same time, however, as they are chemically incompatible. In chronic cystitis with ammoniacal urine hexamethylenamin is without effect, as it is virtually impossible to change the reaction of the urine without causing serious diarrhea with the large doses of acid sodium phosphate.

As the urine of typhoid patients frequently contains typhoid bacilli long after the establishment of convalescence, and as this secretion may be the means of spreading the infection, Horton-Smith Richardson, Gwyn and others advocate as a routine prophylactic measure the administration of hexamethylenamin during the last weeks of the disease. Keyes, Otis and others have found the drug of some value also as a preventive of infection when administered for several days before and several days after *operations on the genito-urinary tract*. It is important, however, that it should not be used too freely, since the excretion of formaldehyd in large amounts tends to retard healing.

Hexamethylenamin has been recommended in infections of the gall-bladder, of the cerebrospinal meninges, of the nose, of the bronchi, etc., but as the amount of formaldehyd yielded by the drug in the body fluids, other than the gastric juice and urine, is too small to exert any antiseptic influence, the recommendation does not seem to rest on a rational basis.

Untoward Effects.—Even therapeutic doses of hexamethylenamin, especially if frequently repeated, may sometimes cause frequent micturition, a burning sensation in the region of the bladder and hematuria, but, as a rule, these symptoms rapidly disappear upon the withdrawal of the drug.

Incompatibles.—Acids, acid salts, tannin, mercuric chlorid and oxidizing agents.

SULPHUR DIOXIDUM

(Sulphur Dioxid, SO_2)

Sulphur dioxid, the anhydrid of sulphurous acid (H_2SO_3), is usually obtained, when required in large quantities, by burning sulphur.

Pharmacologic Action and Therapeutics.—Sulphur dioxid is an intensely irritant, suffocating gas, capable, if inhaled in sufficient quantity, of destroying life. In the presence of moisture it has some power as a germicide, and before the introduction of formaldehyd it was the most popular gaseous disinfectant for rooms, hospital wards, ships, etc. Formaldehyd, however, being more reliable and without injurious effects on colored fabrics, has almost entirely displaced it. As it is destructive to insects, it is preferable to formaldehyd as a disinfectant in the control of malaria, yellow fever and other mosquito-borne diseases. For the gas to be at all effective, at least 4 pounds of sulphur should be burned for every 1000 cubic feet of air-space in the apartment. The sulphur, in the form of small fragments, should be put in a pan, and the latter should be placed inside of a tub partly filled with water. Before being ignited the fragments should be well saturated with alcohol. To secure the required amount of moisture steam may be generated at the same time or the walls and contents of the room may be previously sprayed with water. Key-holes and other openings should be carefully sealed, and the gas should be allowed to act for from ten to twelve hours.

A more convenient method of sulphurous acid disinfection, but one not always available, is to use the gas that has been liquefied under pressure and has been stored in metal cylinders.

SODII THIOSULPHAS, U. S. P.

(Sodium Thiosulphate, Sodium Hyposulphite, $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$)

Sodium thiosulphate, or sodium hyposulphite, occurs in white, transparent prisms, odorless, and of a cooling, somewhat bitter taste. It is freely soluble in water. The dose is from 5 to 20 grains (0.3–1.3 gm.).

Therapeutics.—It is an excellent unirritating parasiticide in ringworm—*tinea circinata* and *tinea sycosis*—and in *tinea versicolor*. It may be applied either as a lotion or as an ointment in the strength of a dram (4.0 gm.) to the ounce (30.0 mls or gm.). It is also effective in *ivy-poisoning*, in which it may be prescribed as follows:

℞. Sodii thiosulphatis..... ʒj (30.0 gm.)
 Glycerini..... f ʒss (15.0 mls)
 Aquæ..... q. s. ad f ʒ viij (240.0 mls).—M.
 Sig.—Keep constantly applied.

A solution of 30 grains (2.0 gm.) to the ounce (30.0 mls) makes a useful **mouth-wash** in *thrush*. Internally, it has been found of service as an antiseptic in *gastreclasis*, when sarcinæ and yeast are present in large quantities in the stomach-contents.

Sodii Sulphis, U. S. P. (Sodium Sulphite; $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O}$) and **Sodii Bisulphis**, U. S. P. (Sodium Bisulphite; NaHSO_3 .) These salts are sometimes employed as substitutes for sodium hyposulphite.

LIQUOR HYDROGENII DIOXIDI, U. S. P.

(Solution of Hydrogen Dioxid, Solution of Hydrogen Peroxid)

Hydrogen dioxid (H_2O_2) is a very unstable compound, prepared by the action of mineral acids or barium dioxid. It is employed in medicine only in the form of aqueous solutions. The official solution, when freshly prepared, contains about 3 per cent., by weight, of the pure dioxid, an amount corresponding to about 10 volumes of available oxygen. This solution is a colorless liquid, odorless, of a slightly acidulous taste, and producing a foam in the mouth. Sunlight, protracted agitation, heat, and many metallic substances serve to decompose it into oxygen and water.

Pharmacologic Action and Therapeutics.—The therapeutic value of hydrogen dioxid depends upon the readiness with which it parts with oxygen when it is brought in contact with the tissues and fluids of the body. When it is applied to a suppurating wound, effervescence follows from the liberation of oxygen, the pus is discharged, and the surface is left perfectly clean and protected by a delicate coagulum. When taken internally it causes no special symptoms, its decomposition into oxygen and water being speedily effected in the stomach. According to Egbert, it has no inhibitive influence on the unorganized ferments, such as ptyalin and pepsin. When injected intravenously or subcutaneously, however, it may kill suddenly by forming gaseous emboli in the blood. The same accident has also resulted from its introduction into one of the large serous sacs. Owing to its oxidizing power also it is an active germicide and deodorant. A 20 per cent. solution of the official preparation quickly destroys pyogenic cocci and other non-spore-bearing bacteria. As an antiseptic for general surgical purposes its drawbacks are its proneness to deteriorate and the rapidity with which it is rendered

inert by contact with organic matter; its advantages are its freedom from odor and toxic properties. It is slightly irritant.

Hydrogen dioxid is useful in the preliminary treatment of *septic wounds*, *abscess cavities*, and *fistulous tracts*; its efficacy in these cases being due in part to its antiseptic action and in part to its mechanical action in expelling pus, bloodclots, and detritus. It is generally applied diluted with from 1 to 3 parts of water. It should not be injected into deep abscesses, unless there is a free exit for the gas and pus, as otherwise serious harm may result from the increased tension within the cavity; neither should it be introduced, under any circumstances, into a large serous sac, such as the pleura or peritoneum.

A 25 to 50 per cent. solution of the official preparation makes a satisfactory wash or spray for the nose and throat in *diphtheria*. If an atomizer be used, the tube and nozzle should be of hard rubber or of glass, as contact with metal favors the decomposition of the dioxid. A solution of the same strength is also serviceable in *mercurial stomatitis*, in *noma*, and in *follicular tonsillitis*. Harris has found copious rectal injections of a dilute solution (1:4 or 8) of some benefit in *amebic dysentery*.

The bleaching properties of hydrogen dioxid render it useful, according to Bulkley, in *hiding superfluous black hair* upon the face of women. Its physical action also makes it useful in removing the particles of carbon in gunpowder burns.

With the hope that it might impart some of its oxygen to the blood, it has been recommended internally in a number of diseases, but in none has it gained any reputation. It may be used, however, as an antidote in *cyanid* and *phosphorus-poisoning*.

POTASSII PERMANGANAS, U. S. P.

(Potassium Permanganate, KMnO_4)

Potassium permanganate occurs in the form of slender, dark-purple prisms, odorless, and of a sweetish, astringent taste. It is soluble in 13.5 parts of water, and is decomposed by alcohol. The dose is from 1 to 3 grains (0.06–0.2 gm.) in pill form, after meals.

Pharmacologic Action and Therapeutics.—In concentrated solution potassium permanganate acts as an irritant or mild caustic. By the mouth, if the dose be sufficiently large, it produces the symptoms of a corrosive poison. In the presence of organic matter it quickly yields its oxygen; hence it is a prompt germicide and deodorant. Unfortunately, its usefulness is considerably restricted by the facility with which it is rendered inert by deoxidation. Solutions of potassium per-

manganate, however, make valuable deodorizing and detergent washes in many diseases attended with offensive discharges; thus, solutions of from 1 to 3 grains (0.06–0.2 gm.) to the ounce (30.0 mils) may be used with advantage in *gangrenous stomatitis*, *cancer of the tongue*, *ozena*; *cancer of the uterus*, *foul ulcers*, and *bromidrosis*. A warm saturated solution makes a good *disinfectant for the hands*, provided it be followed by a saturated solution of oxalic acid to reinforce the permanganate and to remove the stain. A solution of from 1:6000 gradually increased to 1:1000, used by irrigation or by injection, is quite efficacious in *gonorrhea*. A hot 2 per cent. solution, thoroughly applied, is very efficient in *ivy*, *sumac* and *oak poisoning*. It acts by oxidizing the active principle of these plants, which is an acid resin (toxicodendrol).

Internally, potassium permanganate is used as an *emmenagogue* (see p. 264) and as an antidote to *phosphorus*, *hydrocyanic acid* and *morphin poisoning* (see p. 91).

Incompatibles.—Potassium permanganate has an exceedingly wide range of incompatibilities. With oxidizable substances, especially organic ones, such as alcohol and glycerin, it is explosive.

CALX, U. S. P.

(Lime, Quicklime, Burned Lime, CaO)

Lime is obtained by burning the purest natural varieties of calcium carbonate. It occurs in hard, white lumps, odorless, and of a sharp, caustic taste. It is soluble in 840 parts of water and is insoluble in alcohol. In the presence of water it evolves heat, and is gradually converted into calcium hydrate or slaked lime. Mixed with 3 or 4 parts of water, it forms a magma which is known as milk of lime.

PREPARATIONS

DOSE

Liquor Calcis, U. S. P.....	½–2 fl. oz. (15.0–60.0 mils)
Linimentum Calcis, U. S. P. (Carron oil: equal parts of lime water and linseed oil).	
Potassa cum Calce (Vienna paste; 50 per cent. of each).	

Pharmacologic Action and Therapeutics.—Locally, lime is a quickly acting but superficial escharotic. It is never employed by itself as a caustic, but in the form of potassa cum calce it is occasionally used to destroy *small epitheliomata*. When thoroughly mixed with putrefying matter, quicklime favors disintegration, dispels offensive odors, and acts directly to a limited extent as a disinfectant. Freshly prepared milk of lime

is sometimes employed to disinfect fecal discharges. Calcium hydrate, in the form of lime-water (see p. 191) is used as a mild antacid.

ACIDUM BORICUM, U. S. P.
(Boric Acid, Boracic Acid, H_3BO_3)

Boric acid occurs as colorless, transparent, pearly scales or crystals or as a white, bulky powder, odorless, and of a bitterish taste. It is soluble in 18 parts of water, 18 of alcohol, or 4 of glycerin. The dose is from 5 to 15 grains (0.3–1.0 gm.).

PREPARATIONS

Glyceritum Boroglycerini, U. S. P. (contains 31 per cent. of boric acid in glycerin)

Unguentum Acidi Borici, U. S. P. (10 per cent.)

Liquor Antisepticus (contains 2 per cent. of boric acid, 0.1 per cent. of benzoic acid, 0.1 per cent. of thymol, 25 per cent. of alcohol, and minute quantities of eucalyptol, oil of peppermint, oil of gaultheria, and oil of thyme).

Pharmacologic Action.—In single moderate doses boric acid produces no appreciable effects. It is rapidly absorbed, but somewhat slowly excreted, so that cumulation occurs when it is ingested or absorbed freely for a long time. Excretion takes place chiefly through the urine. In very large doses it acts as an irritant poison, producing symptoms of acute gastro-enteritis and nephritis, an erythematous skin eruption, and collapse. Its continued use in doses of a dram (4.0 gm.) a day not infrequently leads to a train of symptoms to which the term *borism* has been applied. The most important features of this condition are digestive disturbances, marked dryness of the skin and mucous membranes, a tendency to alopecia, erythematous or eczematous eruptions, areas of local edema, albuminuria, and cachexia. The same phenomena have also been observed after repeated external applications and rectal injections of boric acid. Although Annett found that kittens could not live longer than four weeks if fed upon milk containing small quantities of boric acid, it is the opinion of most experimenters (Rideal and Foulerton, Chittenden and Gies, Tunnicliffe and Rosenheim, Vaughan and Veenboer) that the drug when used as a food preservative does not, at least in adults, unfavorably affect nutrition.

Boric acid is a feeble antiseptic, even saturated aqueous solutions having scarcely more than a detergent action. Solutions, however, are soothing rather than irritant, and, unless used in large quantities in cavities from which absorption can readily occur, such as the pleura, colon, or vagina, are virtually non-toxic.

Therapeutics.—As a soothing, cleansing wash, a solution of boric acid (10 gr.—1 fl. oz.—0.6 gm.—30.0 mils) has a wide range of usefulness in *inflammatory diseases of the nose and throat*. A solution of from 5 to 15 grains (0.3–1.0 gm.) to the ounce (30.0 mils) may be employed with advantage as an eye-wash in *simple conjunctivitis* and during *operations on the eye*. Insufflations of boric acid are valuable in *chronic otorrhea*; in acute inflammation of the middle ear, however, especially when the discharge is profuse and contains much mucus, the drug may prove dangerous by clogging the outflow. Daily injections into the bladder of a warm solution (5:10 gr. to 1 fl. oz.—0.3–0.6 gm. to 30.0 mils) are often useful in *cystitis*. Lotions, ointments, and dusting-powders containing boric acid are extensively used in many acute inflammatory skin diseases, such as *erythema intertrigo*, *eczema*, *superficial burns*, and *miliaria*. In *pruritus* a lotion of boric acid and phenol frequently affords relief.

R̄.	Phenolis.....	℥xx (1.2 mils)
	Acidi borici.....	gr. xl (2.6 gm.)
	Glycerini.....	f ℥iss (6.0 mils)
	Aquæ.....	q. s. ad f ℥iv (120.0 mils.).—M.

Dusting-powders containing boric acid are sometimes of service in *bromidrosis*:

R̄.	Pulveris acidi borici.....	℥j (30.0 gm.)
	Pulveris acidi salicylici.....	gr. cc (6.5 gm.)
	Pulveris talci.....	℥iij (90.0 gm.).—M.

The glycerite of boroglycerin is frequently used on vaginal tampons in *chronic endometritis*.

Internally, boric acid is sometimes used in *cystitis with alkaline urine*, but it is less efficacious than acid phosphate of sodium or benzoic acid.

Incompatibles.—Carbonates and bicarbonates.

Sodii Boras, U. S. P. (Sodium Borate; Borax; $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$).—This salt occurs in colorless, transparent prisms or as a white powder, inodorous, and of a sweetish, alkaline taste. It is soluble in 15 parts of water or in 1 part of glycerin, and is insoluble in alcohol. The dose is from 5 to 20 grains (0.3–1.3 gm.). Its action is very similar to that of boric acid, for which it is often substituted. It is incompatible with acids, metallic salts, and alkaloids. Glycerin slowly converts it into boric acid.

Sodii Perboras, U. S. P. (Sodium Perborate; $\text{NaBO}_3 + 4\text{H}_2\text{O}$).—This salt occurs as white crystalline granules or as a powder, odorless, and having a saline taste. It contains 9 per cent. of available oxygen, which it gives off in the presence of

moisture. It is employed as a dusting-powder or in a 2 per cent. solution as a substitute for the solution of hydrogen dioxide.

CARBO LIGNI, U. S. P.

(Wood Charcoal)

Wood charcoal is prepared from any soft wood. To be of the official standard it should be a fine black, odorless and tasteless powder, free from gritty matter. The dose is from 5 to 15 grains (0.3–1.0 gm.).

Charcoal has the property of absorbing many times its own volume of gases or vapors. Owing to the oxygen condensed within its pores it has considerable oxidizing power, which may be utilized to destroy offensive gases, such as hydrogen sulphid, and to hasten the decomposition of organic matter. Thorough wetting destroys its activity. As it is not absorbed when taken internally, it exerts no specific action on the body.

Charcoal is employed chiefly as an absorbent and a deodorant. In the form of a poultice it was at one time a favorite application for *foul ulcers*, but it has been largely displaced by more cleanly dressings. While it is a satisfactory agent for *deodorizing fecal discharges*, it has less disintegrating action than dry earth.

Internally, it is sometimes useful as an absorbent in *flatulent dyspepsia*. It may be given as a powder or in lozenges.

OTHER GERMICIDES, ANTISEPTICS, AND DEODORIZERS

Silver Compounds (see pp. 369–371).—The salts of silver are powerful germicides. Many of the organic compounds are not so irritant as the nitrate, and, moreover, are not affected by albuminous matters or chlorids but they are less strongly antiseptic. They are used especially on mucous membranes.

Bromin (see p. 498).—This substance is an energetic disinfectant, but it is rarely used on account of its destructive and intensely irritant properties. A weak solution (1:400), however, is occasionally employed as a deodorizer for cisterns, trenches, slaughter-houses, etc.

Ferrous Sulphate (see p. 301).—This salt is a very feeble disinfectant. It is sometimes used as a deodorizer for middens, cesspools, etc.

Volatile Oils.—Many of the volatile oils, while they are not actively germicidal, have considerable power as antiseptics. The oils of sandalwood, copaiba, and cubeb (see pp. 252–254) are largely used as genito-urinary antiseptics.

Methyl-blue (Pyoktanin).—This substance, like many of the anilin dyes, has some power as an antiseptic, but very little as a germicide. A solution of 1:1000 has been used with some success in ophthalmic surgery.

Methylene-blue (see p. 454).—This compound, in doses of from 1 to 3 grains (0.06–0.2 gm.), has been used as a urinary antiseptic in gonorrhea. It is also of value as an antimalarial, though it is decidedly inferior to quinin.

Acetanilid (see p. 345).—This compound has been used to some extent as a substitute for iodoform in the treatment of burns and ulcers.

Oxalic acid ($\text{H}_2\text{C}_2\text{O}_4 + \text{H}_2\text{O}$) occurs as transparent, prismatic crystals, having an acid taste. It is readily soluble in water. It is a fairly efficient germicide, and its saturated solution has been recommended by Kelly and others as a *disinfectant* for the hands. In doses of $\frac{1}{4}$ to $\frac{1}{3}$ grain (0.016–0.02 gm.) the drug was at one time used as an emmenagogue, but as it was not very effective and sometimes produced serious symptoms, it was soon abandoned. Talley reported a case of acute poisoning in an anemic girl from the administration of three doses of $\frac{1}{2}$ grain (0.02 gm.) each at intervals of four hours.

Toxicology.—The poisonous properties of oxalic acid do not depend solely upon its corrosive action, for the neutral oxalates may also cause death by paralyzing the central nervous system. The resemblance of the drug to Epsom salt has led to many fatal mistakes. When swallowed in a concentrated form it causes the usual symptoms of an irritant poison; when taken in dilute form it is absorbed and induces muscular weakness, cyanosis, coma, and collapse. The chemical antidote is chalk or lime, which acts by forming an insoluble and inert calcium oxalate. The salts of potassium and sodium cannot be used as antidotes, since they form soluble and poisonous oxalates. Poisoning from the use as foods of sorrel and rhubarb leaves, which are rich in oxalic acid, has been reported.

Ethyl-hydrocuprein (Optochin).—This is a synthetic derivative of cuprein, an alkaloid from cuprea bark (*Remijia pedunculata*). In its chemical structure it is closely related to quinin, the latter being methoxycinchonin, while optichin is ethylhydroxycinchonin. The drug is more toxic than quinin, although its actions are qualitatively similar. *In vitro* it has a specific bactericidal action on pneumococci and when injected into animals usually protects them against artificial pneumococcus infection. In large doses, ethyl-hydroxycuprein has a pronounced tendency to produce retinal changes (ischemia, edema,

and degeneration), which result in temporary or permanent blindness.

The hydrochlorid, in doses of 7 grains (0.5 gm.) three times a day, its effects being carefully observed, has been used to some extent in *lobar pneumonia*, but with no marked success. Moreover, a serious drawback to the use of the drug is the liability to amblyopia, which may last several weeks or months, and which in some instances is permanent.

Locally, ethyl-hydroxycuprein has proved useful in *pneumococcus infections of the eye*, especially in serpigenous corneal ulcer. A 1 per cent. solution in bland oil may be applied every hour. The drug is slightly irritant, anesthetic and antiseptic.

Eukupin and Vuzin.—These names are applied to alkyl derivatives of hydrocuprein. Their actions resemble those of hydrocuprein and quinin, but they are less toxic than the former. Locally, they are antiseptic, analgesic and slightly irritant. Solutions of the bihydrochlorid in the strength of $\frac{1}{2}$ to 1 per cent. have been successfully employed as antiseptics in general surgery. Solutions of $\frac{1}{10}$ per cent. produce anesthesia of the cornea lasting about an hour (Sollmann).

ANTIMALARIALS

Antimalarials are drugs that exert a curative influence in malaria by acting destructively upon the specific parasites present in the blood. The *alkaloids of cinchona*, especially *quinin*, are by far the most important members of this class. *Methylene-blue* and *Warburg's tincture* (Tinctura Antiperiodica), while they have some virtue, do not approach quinin in efficiency. *Arsenic*, although useful in correcting the anemia caused by the parasites, probably has no specific action in the doses usually employed. Some success has been reported from the use of arsphenamin, however, and this may be the result of the specific action of the arsenic.

Many other drugs have been recommended as antimalarials, but they have not proved trustworthy.

CINCHONA, U. S. P.

(Peruvian Bark)

Cinchona* is the bark of *Cinchona Calisaya* and other species of *cinchona*, tall evergreen trees indigenous in South America, and at present largely cultivated in India, Java, and Jamaica.

*Cinchona was first introduced into Europe in 1640 and received its name from the Countess Chinchon, wife of the Peruvian Viceroy, who was cured of a fever by it.

Its activities depend upon a number of alkaloids, the most important of which are *quinin*, *quinidin*, *cinchonin*, and *cinchonidin*. To be up to the official standard, the bark should contain at least 5 per cent. of alkaloids.

In addition to its alkaloids, cinchona contains quinic acid, quinovic acid, and cinchotannic acid.

PREPARATIONS	DOSE
Fluidextractum Cinchona, U. S. P.....	10 to 30 min. (0.6–2 mils)
Tinctura Cinchona, U. S. P.....	$\frac{1}{2}$ to 1 fl. dr. (2.0–4.0 mils)
Tinctura Cinchonæ Composita, U. S. P. (Huxham's Tincture:* red cinchona, 10; bitter orange-peel, 8; serpentaria, 2).....	$\frac{1}{2}$ to 1 fl. dr. (2.0–4.0 mils)

The following alkaloidal compounds are also used medicinally:

PREPARATIONS	DOSE
Quinina, U. S. P.....	1–10 gr. (0.06–0.6 gm.)
Quininæ Sulphas, U. S. P.....	
Quininæ Bisulphas, U. S. P.....	
Quininæ Hydrochloridum, U. S. P.....	
Quininæ Dihydrochloridum, U. S. P.....	
Quininæ Hydrobromidum, U. S. P.....	
Quininæ Salicylas, U. S. P.....	2–15 gr. (0.13–1.0 gm.)
Quininæ Tannas, U. S. P.....	
Quininæ et Ureæ Hydrochloridum, U. S. P.....	(Subcutaneously) 15 gr. (1.0 gm.)
Cinchoninæ Sulphas, U. S. P.....	2–15 gr. (0.13–1.0 gm.)
Cinchonidinæ Sulphas, U. S. P.....	2–15 gr. (0.13–1.0 gm.)
Quininæ Ethylcarbonas (Euquinin).....	2–15 gr. (0.13–1.0 gm.)
Aristochin (Diquinin carbonic ester).....	2–15 gr. (0.13–1.0 gm.)

Quinin also enters into iron and quinin citrate, syrup of the phosphates of iron, quinin, and strychnin, compound syrup of hypophosphites, elixir of iron, quinin and strychnin phosphates, and Warburg's tincture.

Quinin is the most important alkaloid of cinchona, and represents very largely its active properties.

Of the salts, the most soluble are the dihydrochlorid (1 in 0.6 part of water), quinin and urea hydrochlorid (1 in 0.9 part of water), and the bisulphate (1 in 9 parts of water). The sulphate is soluble in 725 parts water and the tannate and the ethylcarbonate are almost insoluble in water.

QUININA, U. S. P.

(Quinin)

Quinin occurs in the form of a white micro-crystalline powder, odorless and having an intensely bitter taste. It is almost

* John Huxham (1692–1768), an English physician of Devon and one of Boerhaave's pupils, devised this tincture.

insoluble in water, but is readily soluble in acidulated water, alcohol or ether.

Pharmacologic Action.—Large doses of quinin (15 gr.—1.0 gm.), and even small doses in susceptible persons, cause a sense of fulness in the head, ringing in the ears, impairment of hearing, and sometimes dimness of vision. The term *cinchonism* is applied to this group of symptoms. Toxic doses may cause in addition circulatory depression, dyspnea, delirium, stupor, convulsions and coma.

Although alarming symptoms have been produced by overdoses of quinin, it is doubtful whether death has ever resulted directly from the oral administration of the drug. Death has occurred, however, from the intravenous injection of quinin.

Local Action.—Quinin is irritant and when administered subcutaneously causes pain and sometimes local necrosis or an abscess. The double salt of quinin and urea hydrochlorid is less irritant than most of the other salts. When this compound or any other very soluble salt of the alkaloid is applied directly to a mucous membrane or is injected beneath the skin, it depresses the sensory nerve endings and produces persistent anesthesia.

Action on Lower Organisms.—Quinin is a protoplasmic poison, its action being especially marked on motile cells, such as leucocytes, spermatozoa, amebæ, etc. In malaria it is definitely parasitotropic. The drug is not an efficient bactericide, except in strong solutions, but it is an antiseptic of considerable power, a solution of 1:800 inhibiting the growth of bacteria in fluids containing much organic matter.

Absorption and Excretion.—Quinin is absorbed from the intestine, and under favorable conditions it enters the blood rapidly. It is excreted chiefly by the kidneys, and traces of it may be found in the urine within twenty minutes after its ingestion. The excretion of the drug, however, does not quite keep pace with its absorption, and after large doses several days may elapse before all of it has left the body. A large amount is completely destroyed in the tissues.

Circulatory System.—Moderate therapeutic doses of quinin have little or no effect on the circulation in healthy persons, but very large doses first quicken the pulse and raise the blood-pressure and then slow the pulse and lower the bloodpressure. These effects are probably due to a primary stimulation of the heart itself and the arterial muscle, and a secondary depression of the same structures. The vessels of the cerebrum and internal ear appear to be especially susceptible to the vasodilating action of the drug.

In auricular fibrillation quinin, and more particularly its isomer quinidin (see p. 452), often lessen the excitability of the auricle and restore normal rhythm.

Nervous System.—The cerebral symptoms resulting from large doses of quinin are probably due to local circulatory changes. The drug has a slight central analgesic action, similar to but much less pronounced than that of antipyrin and acetphenetidin. The tinnitus aurium and deafness occurring in cinchonism seem to be due to congestion of the middle ear and labyrinth. In rare instances deafness has become permanent, apparently owing to chronic inflammation of the middle ear, hemorrhage into the labyrinth, or to secondary degenerative changes in the spiral ganglia. Quinin amblyopia or amaurosis is supposed to be due to constriction of the retinal vessels, although there is some evidence to show that it is the result of a specific toxic effect on the retinal cells. Occasionally, the impairment of vision or blindness is permanent.

Toxic doses of quinin first stimulate the respiratory center and then depress it. Fatal doses usually kill through paralytic asphyxia. The drug has virtually no action on the spinal cord in man, but in frogs it first increases and then decreases the reflex excitability. Very soluble salts of quinin, such as quinin and urea hydrochlorid, when injected subcutaneously, depress the sensory nerve-endings and produce a local anesthetic effect, which is much more persistent than that of cocain.

Alimentary Canal.—In small doses, taken before meals, quinin, owing to its bitter taste, acts as a stomachic. Large doses retard the action of the digestive ferments and may excite nausea and vomiting.

Uterus.—Quinin intensifies labor-pains when they are inefficient owing to general weakness or fatigue. The contractions induced by it are less prolonged than those following the use of ergot, but are apparently caused by the direct action of the drug on the uterine muscle. Quinin does not seem to be capable, in ordinary doses, of originating labor-pains and acting as an abortifacient.

Blood.—As Binz originally noted, quinin, when added to freshly drawn blood, arrests the ameboid movement of the white cells. Moreover, when applied in very dilute solution to the exposed mesentery of a frog, it suspends, almost immediately, the migration of the leukocytes. These effects are ascribed to the toxic action that the drug exercises on all forms of undifferentiated protoplasm. Drawn blood, when mixed with quinin, loses in oxidizing power, as shown by its failure to strike a blue

color with guaiac in the presence of turpentine and to decolorize indigo by transforming it into isatin.

Metabolism.—Under the influence of quinin there is a considerable falling off in the nitrogenous excretion, and as this continues even when the patient is fasting, it is apparently due to diminished protein metabolism and not to diminished utilization of food.

Temperature.—In health the bodily temperature is not appreciably influenced by quinin; in fever, however, large doses of the drug exert a pronounced and somewhat persistent antipyretic effect. The reduction of temperature occurs in animals after section of the spinal cord, and therefore it is not the result of any action exerted on the heat-regulating centers. It is undoubtedly a peripheral effect, and is to be ascribed to depression of protein metabolism and consequent diminished heat production.

Untoward Effects.—Idiosyncrasies to quinin are not infrequently encountered. In some individuals a dose of from 2 to 3 grains (0.1–0.2 gm.) will cause intense cinchonism. Impairment of vision is fortunately rare, and has generally been produced by very large doses. Quinin rashes are not uncommon; of 60 cases analyzed by Morrow, 38 were erythematous, 12 urticarial, 5 purpuric, and 2 vesicular and bullous. Irritability of the bladder and urethra is occasionally noted.

Quinin is not directly hemolytic, but the cases on record in which hemoglobinuria could be produced at will by the use of the drug make it appear reasonably certain that in some individuals it may act as an auxilliary factor in producing hemolysis and hemoglobinuria.

Idiosyncrasy may be determined by applying a drop of a 1 to 10 per cent. solution of quinin to the scarified skin. The occurrence of edema with a wide zone of erythema in about 5 minutes indicates abnormal susceptibility to the drug.

Therapeutics.—Owing to its destructive action on the parasites of *malaria*, quinin is to be regarded as a specific in this disease. The tertian and quartan parasites, as a rule, readily succumb to it, but the estivo-autumnal parasite (*Plasmodium falciparum*) is more resistant, especially when in the crescentic or ovoid form. In ordinary *tertian* and *quartan* infections 30 grains (2.0 gm.) a day will usually arrest the paroxysms within a few days. As the drug is most effective when the young ameboid forms (trophozoites) are still free in the blood-plasma, it is usually advisable to give 15 grains (1.0 gm.) of the daily dose toward the close of the paroxysms, that is when the temperature is beginning to fall. However, if the patient is seen some time after a chill, and another is not expected for 36 hours or more, it is better

to begin treatment at once and to give a smaller dose of quinin (10 grains-0.65 gm.) three times a day. The drug should be continued in such amounts until the paroxysms entirely cease, and then given in the dose of 10 grains (0.65 gm.) once a day for at least 2 months. The administration of a laxative dose of calomel seems to increase the efficiency of the quinin, probably by promoting absorption. During convalescence iron and arsenic may be advantageously associated with the quinin.

In *estivo-autumnal (subtertian) infection* somewhat larger doses of quinin than are required in tertian and quartan malaria are often necessary. About 40 grains (2.6 gm.) a day, however, usually suffices. In *pernicious malaria* rapid action is imperative, and, therefore, the drug should be given intramuscularly, or, better still, intravenously.

Whether the administration of quinin is at times responsible for the occurrence of *hemoglobinuria* in malarial subjects, as was first suggested by Verétas in 1858, is still a mooted question. Even if the affirmative be true, there does not seem to be any good reason for withholding the drug in cases of hemoglobinuria when malarial parasites can be detected in the blood. Bastianelli has summed up the matter in the following rules: If hemoglobinuria occurs during the paroxysms and parasites are found, use quinin; if parasites are not found, do not use quinin; if quinin has been used before the hemoglobinuria begins and there are no parasites, discontinue the quinin.

Quinin is not only a curative remedy in malaria, but it is also of considerable value as a *prophylactic agent*. Doses of 5 grains (0.3 gm.) daily and a double dose once a week (Castellani), or of 3 grains (0.2 gm.) each morning and evening (Celli) frequently prevent the occurrence of the disease in persons living in malarial regions, although some authorities believe that in the event of failure there is danger of producing immunity to quinin on the part of the parasites.

Quinin in doses of from 1 to 2 grains (0.06-0.13 gm.) has long been used as a general tonic in *states of lowered vitality* following acute disease or brought on by overwork. In such cases it may often be combined advantageously with iron and strychnin. Small doses are thought to be of some value also in *acute infections*, such as septicemia, influenza, etc. It is possible that the drug owes its efficacy in these diseases to its power to lessen metabolism. Warm rectal injections of the alkaloid (1:3000 to 1:1000) have been used with some success in *amebic dysentery*. In *whooping-cough* moderately large doses are sometimes useful in lessening the severity and frequency of the paroxysms, but it is not known how the drug acts. Quinin is often employed in small

doses for its analgesic effect in "colds," *neuralgia*, *acroparesthesia*, etc.

The use of quinin as an *antipyretic* is virtually obsolete. In doses of from 20 to 30 grains (1.3–2.0 gm.) it has a pronounced effect upon high temperature, especially if it is given an hour or two before a natural remission is expected to occur, but when a drug must be used at all as an antipyretic, the preference should usually be given to one of the benzol derivatives (acetphenetidin, antipyrin, etc.), owing to the promptness and certainty of its action and its comparative freedom from unpleasant side-effects.

Quinin in doses of from 10 to 15 grains (0.6–1.0 gm.) is sometimes of service as an *ecbolic* (see p. 270) in labor when the pains are infrequent and inefficient, owing to *simple uterine inertia*.

A solution of quinin and urea hydrochlorid ($\frac{1}{4}$ per cent.) may be used instead of cocain in producing *infiltration anesthesia*. The effect lasts several hours. Stronger solutions (1–3 per cent.) produce anesthesia lasting several days, but they are likely to result in fibrous induration. Owing to its persistent effect, the drug is especially useful in operations about the anus.

Contraindications.—The chief contraindications are *idiosyncrasy*, inflammation of the middle ear, and *meningitis*. It must be used cautiously when acute inflammation of the urinary tract is present. There is some evidence to show that the drug sometimes acts unfavorably in epileptics in increasing the number of paroxysms.

Administration.—Under ordinary circumstances quinin should be given by the mouth. It may be prescribed in capsules, cachets, freshly made pills, or in solution. The last method of prescribing it, however, is objectionable on account of its intensely bitter taste. Old pills should be avoided, since they are liable to escape from the bowel before the alkaloid has been liberated and absorbed. The sulphate seems to be as effective as any other salt, although it is less soluble than the dihydrochlorid and the bisulphate. The sulphate may be rendered soluble by combining it with a few drops of hydrochloric acid.

To children, the drug may be given suspended in syrup of yerba santa, syrup of chocolate, or elixir of licorice. The tannate, while it has less than half of the alkaloidal strength of the sulphate, is only slightly bitter, and may, therefore, be given to children in the form of chocolate tablets. Euquinin is a tasteless and insoluble preparation, somewhat more active than the tannate.

Quinin is absorbed very imperfectly from the rectum, but for young children it may be prescribed in the form of suppositories,

each containing 2 or 3 grains (0.13–0.2 gm.) of a soluble salt, such as the dihydrochlorid.

For intramuscular injection only the most soluble salts should be used, such as quinin and urea hydrochlorid and the dihydrochlorid. Bacelli's formula is satisfactory. It consists of 10 grams of the dihydrochlorid and 0.075 grams of sodium chlorid dissolved in 10 grams of water. One-tenth of the solution is used for each injection, which may be made in the gluteal region. For intravenous injection the maximum dose is 10 grains (0.65 gm.) of a soluble salt in 200 mls of normal saline solution. Larger doses and higher concentrations are distinctly dangerous, especially if the patient's bloodpressure is low. As a rule, the daily dose should not exceed 30 grains (2.0 gm.). The solution should be sterile and injected very slowly, according to the technique used in administering arsphenamin.

Of the preparations of cinchona itself, the tincture and the compound tincture are sometimes employed as a tonic in convalescence from acute infectious diseases.

Incompatibles.—Alkalis, tannin, iodids, salicylates, spirit of nitrous ether.

Cinchonin and Cinchonidin.—These alkaloids have actions similar to those of quinin, but they are more toxic and less efficient as antimalarials.

QUINIDIN

Quinidin, an isomer of quinin, has actions similar to those of quinin, although apparently its effect upon the cardiac muscle is more pronounced. In appropriate doses it may actually abolish auricular fibrillation or auricular flutter by depressing excitability and conduction in the auricular muscle. Digitalis does not control fibrillation itself, but it tends to lower the rate of the ventricular contractions and to restore the normal rhythm by depressing the conductivity of the auriculoventricular bundle. Quinidin, on the other hand, restores normal rhythm in the fibrillating auricle itself in about 50 per cent. of the cases, but at the same time it actually increases the ventricular rate, the latter sometimes reaching 120 to 160 per minute.

The drug has given the best results in the *prevention of paroxysmal auricular fibrillation, and in the removal of persistent fibrillation of comparatively recent origin in patients who have had but little cardiac enlargement and little or no cardiac failure.* Cases of multiple valvular lesions or of pronounced mitral

stenosis are much less likely to respond with normal rhythm. Unpleasant symptoms, such as headache, palpitation, precordial discomfort, nausea or vomiting, dizziness, and diarrhea, not infrequently follow the use of the drug, and occasionally, sudden collapse, ventricular tachycardia and heart failure, or embolism (cerebral, pulmonary, peripheral, or other) occurs. The occurrence of embolism is due to the loosening of auricular thrombi by the reestablishment of normal contractions in auricles, the action of which has been paralyzed by fibrillation.

Quinidin therapy is still in the experimental stage and considerable caution must be exercised in applying it. As a safeguard against accidents, it is advisable for the patient to be in bed and under close observation while the treatment is being carried out. The drug, in full doses, is unsuitable for ambulatory patients. Pronounced dilatation of the heart with symptoms of venous stasis, symptoms or signs of recent embolism, acute or recurrent endocarditis, angina pectoris, heart-block, and quinid idiosyncrasy contraindicate the use of quinidin.

In a few instances quinidin has proved useful in preventing the occurrence of *paroxysmal tachycardia* and in causing the disappearance temporarily of *ectopic beats*.

Administration.—Two doses of 3 grains (0.2 gm.) each of the sulphate or bisulphate are given on the first day as a test for idiosyncrasy, and then, if there are no toxic symptoms, the dose may be increased to 4 or 6 grains (0.26–0.4 gm.), three or four times a day, until the rhythm becomes regular or toxic symptoms appear. The treatment should be suspended if severe headache, dizziness, palpitation, precordial distress, or other untoward symptoms develop. An auricular rate below 250 or 240 per minute and, as a rule, a ventricular rate above 160 also contraindicate the further administration of the drug (Lewis). If fibrillation still continues after 2 or 3 days of treatment it is usually advisable to discontinue the quinidin treatment, as after this period the likelihood of success is remote. The shorter the duration of the fibrillation, the less is the amount of quinidin necessary to restore normal rhythm (White). Relapse occurs in from a few days to several months in the large majority of cases of persistent fibrillation. A daily dose of 6 grains (0.4 gm.) often suffices to prevent relapse after the return to normal rhythm, and, especially, to prevent recurrences in the paroxysmal form of fibrillation. If there is any degree of decompensation it is always advisable to restore the circulation with digitalis before using quinidin. Digitalis is also useful after quinidin treatment in controlling the ventricular rate, if this is unduly rapid.

Quinidin is best administered in gelatin capsules.

METHYLTHIONINÆ CHLORIDUM, U. S. P.

(Methylthionin Hydrochlorid, Tetramethylthionin Hydrochlorid, Methylene-blue, $C_{16}H_{18}N_3SCl$)

Methylene-blue is a complex anilin derivative, occurring in dark-blue crystals or as a bronze-like powder, readily soluble in water or in alcohol. The dose is from 1 to 4 grains (0.065–0.26 gm.). When taken by the mouth or injected subcutaneously, it enters the blood and soon reappears in the secretions, especially in the urine, to which it imparts an intensely blue or greenish-blue color. Large doses irritate the stomach and also excite frequent and painful micturition.

The fact that methylene-blue is one of the best stains for the hematozoa of *malaria* suggested its use as a remedy in this disease. While it undoubtedly has some value, its efficacy is decidedly inferior to that of quinin. It may be used with advantage, however, when, owing to an idiosyncrasy, quinin cannot be taken. Flint found it of service in cases of *filariasis*, but in a case studied by Henry it was without effect. The drug appears to be of some value as an antiseptic in inflammatory diseases of the genito-urinary tract, especially in *gonorrhea*.

The strong affinity shown by Ehrlich to exist between the axis-cylinders of nerves and methylene-blue prompted the use of the drug as an analgesic and a sedative. It has been employed as an analgesic by Lemoine, Klemperer, and others with asserted good results in *neuralgia*, *sciatica*, and *migraine*, and as a sedative by Bodoni and others in various forms of *insanity characterized by excitement*.

Methylene-blue should be prescribed in pills or capsules, combined with half its weight of powdered nutmeg, the latter serving to prevent colic. Patients should always be warned of the discoloration of the urine caused by the drug.

WARBURG'S TINCTURE

(Antiperiodic Tincture)

Warburg's tincture was for a time a proprietary preparation, but in 1875 the originator himself made known its composition. As a number of the ingredients recommended by Warburg are no longer obtainable, the remedy is at the present day prepared after a somewhat simpler formula than the original one. Each fluidounce (30.0 mls) contains: quinin, 10 grains (0.65 gm.); rhubarb and angelica seed, of each, $3\frac{1}{2}$ grains (0.2 gm.); elecamp-ane, saffron, fennel, and extract of aloes, of each, $1\frac{1}{3}$ grains (0.1 gm.); gentian, zedoary, cubeb, myrrh, white agaric, and camphor, of each, $\frac{7}{8}$ grain (0.05 gm.).

Warburg's tincture is an active diaphoretic and is somewhat effective as an *antimalarial*, its value in this respect probably depending upon its quinin content. The bowels should first be moved with a saline cathartic and then $\frac{1}{2}$ ounce (15.0 mls) of the tincture should be taken at once, undiluted, no other fluid being taken.

ANTHELMINTICS

Anthelmintics or vermifuges are agents that exert a toxic effect on intestinal worms and facilitate their expulsion. The most important members of the group are:

Tape-worms :

Aspidium	Cusso
Pomegranate	Kamala
Pumpkin-seed	Thymol
Chloroform.	

Round Worms :

Santonin	Oil of Chenopodium
Spigelia.	

Pin-worms or Seat Worms :

Santonin or oil of chenopodium by the mouth and one of the following drugs by rectal injection:

Quassia.	Vinegar
Lime-water	Sodium chlorid
Tannin.	

Hook-worms :

Oil of chenopodium	Thymol
Betanaphthol.	

Anthelmintics are all more or less irritant to the gastro-intestinal tract and when absorbed toxic to the host. They rarely kill the worm, but merely stupefy or paralyze it, so that its hold on the intestinal mucous membrane is loosened and it can be more readily expelled in the stools. A brisk cathartic is therefore always required after an anthelmintic for the purpose of carrying out the weakened parasite. The dosage of anthelmintic remedies is somewhat difficult to gauge, as the amount of the drug must be sufficient, at least, to narcotize the worm and yet not large enough to injure seriously the host. To secure the best results, medication should be preceded by fasting or a light diet for about twelve hours, so that the parasite will be protected as little as possible by intestinal contents.

ASPIDIUM, U. S. P.

(Male Fern, Filix-mas)

Aspidium is the rhizome of *Dryopteris Filix-mas* and of *Dryopteris marginalis*, ferns growing in North America, Europe, and Asia. It contains a fixed oil, a volatile oil, resin, *flicic acid*, and a number of neutral bodies, the chief of which is *aspidin*. Of these, amorphous flicic acid and aspidin are probably the most active constituents.

PREPARATION

DOSE

Oleoresina Aspidii, U. S. P. 1 dr. (4.0 mils).

Pharmacologic Action and Therapeutics.—In overdoses aspidium is an energetic poison, producing abdominal pains, vomiting and purging, vertigo, headache, increased reflex activity, tonic spasms, collapse, and coma. Temporary or permanent blindness has also been present in many of the cases. Of 78 cases of poisoning by male-fern collected by Sidler-Huguenin, in 12 death occurred, and in 18 there was lasting impairment of sight in one or both eyes. According to Okamoto, microscopic examination of the eyes of poisoned dogs shows degenerative changes in the optic nerves.

Aspidium is perhaps the most generally useful remedy for *tape-worm*. A dram (4.0 mils) of the oleoresin may be given in emulsion or in capsules at bedtime, and followed in the morning by a saline purgative. Castor oil should not be used, as oils are believed to increased the toxicity of aspidium by favoring the absorption of its active constituents.

GRANATUM, U. S. P.

(Pomegranate)

Pomegranate is the bark of the stem and root of *Punica Granatum*, a small tree indigenous in Southwestern Asia, and cultivated in most subtropical countries. It contains, in addition to a large quantity of tannin, a number of liquid alkaloids, the chief of which are *punicin* and *iso-punicin*. A mixture of the tannates of the alkaloids in varying proportions is official as *Pelletierinæ Tannas*.^{*} This preparation is a light yellow, odorless, amorphous powder, having an astringent taste. It may be given in doses of 3 to 8 grains (0.2–0.5 gm.).

^{*} This name was given in honor of Joseph Pelletier (1788–1842), who was the discoverer of strychnin, a number of opium alkaloids, and together with Caventou of quinin, together with Magendie of emetin, and together with Couerbe of picrotoxin.

PREPARATION

DOSE

Fluidextractum Granati, U. S. P. $\frac{1}{2}$ –1 fl. dr. (2.0–4.0 mls).

Pharmacologic Action and Therapeutics.—Locally, pomegranate is astringent. Internally, large doses of the bark or of the alkaloids may cause headache, vertigo, dimness of vision, nausea, vomiting, and extreme muscular weakness. The last symptom is said to result from paralysis of the peripheral ends of the motor nerves.

Pomegranate is a reliable remedy for *tape-worm*, ranking next to aspidium in efficiency. The fluidextract or a decoction (20 per cent.) is sometimes used, but these preparations are very unpalatable and less certain in their action than the mixture of alkaloids. Adjuvant treatment is necessary as in the case of the other teniacides.

CUSO

(Kouso, Brayera)

Cusso is the female inflorescence of *Hagenia abyssinica*, an ornamental tree growing in the mountainous districts of Abyssinia. A neutral body, *kosotoxin*, is probably the active principle. It is related to filicic acid. The dose of cusso is from 2 to 4 drams (8.0–16.0 gm.), as an infusion.

Therapeutics.—Cusso, provided it is fresh, is an efficient teniacide. It is, however, very unpalatable and likely to cause nausea and vomiting. As a rule, it does not require the assistance of a purgative, but one should be given if the bowels do not move within six or eight hours.

PEPO, U. S. P.

(Pumpkin-seed)

Pepo is the dried ripe seed of the common pumpkin, *Cucurbita Pepo*. Its active principle has not been isolated, but according to Sollmann it is soluble in water and destroyed by boiling.

Pumpkin-seed is a perfectly safe, but somewhat uncertain, remedy for *tape-worm*. It is usually prescribed in the form of an emulsion, made by beating the decorticated seeds into a paste, adding sugar, and diluting with water or milk. It should be taken in the morning on an empty stomach, and followed in two or three hours by castor oil. The dose is from 1 to 2 ounces (30.0–60.0 gm.).

KAMALA

(Rottlera)

Kamala is a brownish-red, tasteless powder, consisting of the minute glands and hairs from the capsules of *Mallotus philip-*

pinensis, a small tree growing in India, China and the Philippine Islands. It contains several resinous principles, one of which occurs in yellow needles and is known as *rottlerin*. The dose of kamala is from 1 to 2 drams (4.0–8.0 gm.).

Therapeutics.—Kamala has been highly spoken of as a teniacide by East Indian surgeons. It is rarely employed in this country. It is best given suspended in syrup or honey. A purgative is seldom required after it, as the drug itself causes considerable intestinal irritation and diarrhea.

SANTONINUM, U. S. P.

(Santonin)

Santonin is the anhydrid or lacton of santonic acid, a compound obtained from Santonica, or Levant wormseed (*Artemisia pauciflora*), a perennial shrub growing in Turkestan. It occurs as colorless, shining prisms, odorless, and of a slightly bitter taste. It is almost insoluble in water, but readily so in alkaline solutions. The dose for a child is $\frac{1}{2}$ to 1 grain (0.03–0.065 gm.); for an adult, 1 to 3 grains (0.065–0.2 gm.).

Pharmacologic Action and Therapeutics.—Santonin is transformed in the intestine into sodium santoninate, which for the most part is eliminated unchanged in the stools. A small amount, however, is absorbed and imparts to the urine a deep yellow or reddish color. The drug is non-irritant and in therapeutic doses produces no obvious symptoms, except occasionally “yellow vision,” or xanthopsia. The latter is probably the result of a specific action of the drug on the retina. It is certainly not due, as was formerly believed, to staining of the humors of the eye. The drug must be used with caution as poisoning by it has not been uncommon. Santonin-poisoning is characterized by xanthopsia, mydriasis, vertigo, tremors, unconsciousness, and convulsions, first epileptiform and then tetanic. Nausea and vomiting have been observed in some instances. When death results it is usually through asphyxia. The convulsions are due to stimulation of the motor centers—first the cerebral and then the spinal. Death in children has been reported from doses of about 3 grains (0.2 gm.).

Santonin is probably the most efficient remedy available against *round worms*. It does not kill the parasites, but through some inimical influence causes them to migrate to the colon, whence they may be expelled by a cathartic. The drug may be prescribed in lozenges or in powders, mixed with a few grains of sugar. A good plan is to give it in the morning and evening and to follow it next day by a brisk cathartic, such as castor oil or

calomel. For a child under two years the dose should never be more than $\frac{1}{2}$ grain (0.03 gm.); and for a child under five years, never more than 1 grain (0.065 gm.). Santonin has been recommended in certain other affections, notably in amaurosis, amenorrhea, incontinence of urine, and epilepsy, but it has no claims to confidence in any of these conditions.

SPIGELIA, U. S. P.

(Pinkroot)

Spigelia is the rhizome and roots of *Spigelia marilandica*, a perennial herb growing in the Southern United States. It contains a volatile oil, tannin, a bitter principle, and an alkaloid known as *spigelin*.

PREPARATION

DOSE

Fluidextractum Spigeliæ, U. S. P. $\frac{1}{2}$ –2 fl. dr. (2.0–8.0 mls).

Therapeutics.—Spigelia is a fairly efficient, and if reasonable care be used in its administration, a comparatively safe remedy against *round worms*. Its anthelmintic power, however, is inferior to that of santonin. Toxic doses of the drug produce excitement, flushing of the face, swelling of the eyelids, dilatation of the pupils, dimness of vision, and, finally, stupor. Spigelia should always be administered in association with a purge.

CHENOPODIUM

(American Wormseed)

Chenopodium is the fruit of *Chenopodium ambrosioides anthelminticum*, a perennial herb indigenous in Central and South America, and naturalized in the United States. The active principle is a pale yellow volatile oil (*Oleum Chenopodii*, U. S. P.), having a characteristic disagreeable odor and taste. The dose is given as 3 minims (0.2 mil), but four or five times this amount is often prescribed.

Therapeutics.—Oil of chenopodium in doses of 5 to 10 minims (0.3–0.6 mil), three times a day, for two or three days, is an effective remedy against *round worms*. It may be prescribed in capsules or on sugar. As it does not kill the parasites, but merely paralyzes them, its administration should always be followed in three or four hours by a saline cathartic or castor oil. Oil of chenopodium is even more efficacious in *hook-worm infestation* than as a round-worm remedy. It yields better results than thymol and is much safer and much more reliable than betanaphthol. The dose of the drug recommended by the International Health Board Commission is 1.5 mls, divided into 3 parts, 0.5

mil being given at 7, 8, and 9 o'clock in the morning, and followed at 11 o'clock by a purgative dose of Epsom salts. Preliminary fasting is not essential. Two such treatments are said to remove 99 per cent. of worms present. Billings and Hickley recommend that the bowel be moved with a saline on the day before the specific medication is begun, and that on the following morning, beginning at 7 o'clock, oil of chenopodium be given in doses of 15 drops (not minims), every two hours for 3 doses, and followed by 5 drams (18.0 mls) of castor oil and $\frac{1}{2}$ dram of chloroform (2.0 mls), two hours after the last dose of the vermifuge. A second dose of 1 ounce (30.0 mls) of castor oil is given a half-hour later. The chloroform is said to have a synergistic action, while the castor oil apparently diminishes the toxicity of the anthelmintic. These authors believe that oil of chenopodium is especially valuable because it expels not only hook-worms and round worms, but also whipworms, tape-worms and intestinal flukes.

While the doses suggested are relatively safe for patients in good physical condition, they are probably too large for poorly nourished individuals. A number of cases of poisoning have been reported, the symptoms consisting of abdominal pain, vomiting, diarrhea, headache, somnolence, and collapse. Ataxia, convulsions, and coma may also supervene. Death has occasionally occurred. As oil of chenopodium has some cumulative action, at least a week should elapse between courses of treatment.

Recently, Walker and Emrich have reported success from the use of oil of chenopodium in *amebic dysentery*, especially when the parasites are present in the encysted form.

OTHER ANTHELMINTICS

Chloroform (see p. 124).—This drug, in doses of $\frac{1}{2}$ to 1 fluidram (2.0–4.0 mls), has been used to some extent against *tape-worms*, but it is unreliable. It is still used as an adjuvant to oil of chenopodium in hook-worm infestation.

Quassia (see p. 194).—Rectal injections containing quassia are very efficacious in *oxyures*, or *pin-worms*. To secure the best results the lower bowel should first be thoroughly emptied by means of a soap-and-water enema, after which 2 ounces (60.0 mls) of a cold infusion of quassia (1 oz. to 1 pint—31.0 gm.—0.5 L.) should be slowly injected. As the parasites often occupy the cecum and small intestine, as well as the rectum, it may be necessary, in some instances, in order to secure permanent relief, to give also by the mouth an anthelmintic (spigelia or santonin) with a cathartic.

Lime-water, Vinegar, Sodium Chlorid, and Tannin.

These drugs are sometimes used in the form of rectal injections to destroy *pin-worms*. None is quite so efficacious as quassia. They may be used in the following proportions: Lime-water, undiluted; vinegar, 1 to 3; sodium chlorid, 1 dram (4.0 gm.) to a pint (0.5 L.); tannin, $\frac{1}{2}$ dram (2.0 gm.) to a pint (0.5 L.).

Thymol (see p. 412).—This drug, in doses of 30 grains (2.0 gm.) for adults, or 8 to 15 grains (0.5–1.0 gm.) for children, repeated in two hours, one day a week, a saline purge being administered before and after the treatment, is a valuable remedy in *hook-worm disease*. It has also been used with some success as an anthelmintic against *round worms* and *tape-worms*, especially *Dibothriocephalus latus*.

Betanaphthol (see p. 424).—This drug, used in the same way as thymol, but in doses half as large, has been used to some extent in *hook-worm infestation*, but it is less safe and less effective than either thymol or oil of chenopodium.

Carbon Tetrachlorid has been recommended by Hall for the removal of *hook-worms* and *round worms*. He asserts that it is more effective and safer than either oil of chenopodium or thymol. The dose is 3 mils in hard capsules. It has also been successfully employed against *thread-worms*.

ANTITOXINS AND VACCINES

Our knowledge of serum and vaccine therapy has been gained by the study of the subject of immunity.

Immunity.—The inborn insusceptibility of an individual to a disease to which others are commonly susceptible constitutes *natural immunity*. Immunity the result of changes which have taken place in the body during the life-time of the individual is termed *acquired immunity*. The latter may be the result of disease naturally contracted (*unintentional immunity*); or it may be the result of injections of specific microorganisms or their spores in an attenuated form, or of minute doses of virulent, specific microorganisms, or of the dead bacteria with their contained toxins, or of the serum of an animal that has been previously protected from the disease by one of these methods (*intentional or artificial immunity*).

As Ehrlich, Calmette, and others have shown, the power to confer immunity is not confined solely to bacterial toxins, but is shared also by other protein poisons, such as ricin (from castor-oil beans), abrin (from jequirity seeds), and the venom of poisonous serpents. The investigations of numerous observers have

done much to make clear the mechanism of immunity, but much work still remains to be done in this direction. Pasteur reasoned that a second infection was impossible in many diseases, because in the first infection the bacteria had used up substances that were necessary to their growth. This theory at once became untenable when it was shown that the metabolic products of bacteria were as powerful in conferring immunity as the bacteria themselves. Chauveau conceived the idea that the bacteria left material in the body which rendered the tissues unsuitable for subsequent infection. A serious objection, however, to this theory is the fact that the blood-serum of the animal artificially protected is in many cases a good culture-medium for the special bacteria concerned. Metschnikoff was the first to demonstrate that an important factor in the defence of the body against infection is the capacity of the leukocytes to ingest and destroy bacteria (phagocytosis). Later, it was shown that the leukocytes do not readily act as phagocytes unless aided by certain substances in the body-fluids. These substances, to which has been applied to the term *opsonins*, act upon the bacteria in such a way as to make them an easy prey to the leukocytes. The ratio between the average number of bacteria taken up by healthy leukocytes in a mixture of a bacterial suspension with a patient's blood-serum and the average number taken up in a mixture of the same bacteria with normal blood-serum is known as the *opsonic index*. The latter, normally taken as 1.0, is low in most infections. By the injection subcutaneously of measured small quantities of dead bacteria (vaccines or bacterins), it is possible to raise the opsonic power of the blood-serum and so favor phagocytosis.

The studies of Nuttall, Buchner, and others have shown that the blood-serum, in addition to being an auxiliary factor in phagocytosis, possesses in itself to a certain extent the power to neutralize the poisons made by bacteria or to destroy the bacteria themselves. Those substances in the blood which neutralize toxins are known as *antitoxins*, and those which disintegrate and dissolve the bacteria are known as *bacteriolysins*. In certain infections, such as diphtheria and tetanus, immunity is chiefly antitoxic, while in others, such as cholera and typhoid fever, it is mainly antibacterial.

The manner in which these protective bodies act has not yet been clearly explained, but the "lateral-chain" theory of Ehrlich is highly suggestive. This theory presupposes that the protoplasm of the cells contains complex molecules having a comparatively stable central group of atoms, to which are attached much less stable lateral chains of atoms.

These lateral chains have the power of fixing or "anchoring" such toxins for which they have an affinity, a group of atoms of the cell entering into combination with a group of the toxin. These are designated *haptophore* groups. In addition to its *haptophore* group the toxin contains a *toxophore* group, which carries its toxic properties, but this *toxophore* group cannot act upon the cell until the toxin has been anchored to the cell by a union of the *haptophore* groups. The *haptophore* groups of the cells, which are also known as *receptors*, can unite only with the *haptophore* groups of toxins for which they have a special affinity; hence a toxin may prove harmless for the want of a receptor having an affinity for it (natural immunity). In anchoring the *haptophores* of the toxin by means of its receptors the cell suffers a defect, which, according to definite natural laws, is repaired by a new formation of receptors of the same functional quality. Further fixation ultimately leads to the formation of receptors in excess of those previously existing. These extra receptors, separated from the cells and free in the blood-plasma, are the *antitoxins* which unite with the toxins and neutralize them by preventing their union with receptors still attached to the cells.

Two forms of artificial immunity occur: active and passive. Immunity that follows infection or vaccination and is produced through the activity of the animal itself is known as *active immunity*, while that resulting from the direct transference of protective substances from another animal already immune is known as *passive immunity*.

Active Immunization.—This may be achieved not only by the introduction into the body of living virulent organisms, but also through the use of organisms that have lost much of their virulence or are actually dead. Although it brings into action the entire defensive mechanism of the body, active immunization is effected comparatively slowly and therefore it is chiefly useful for prophylactic purposes and in the treatment of infections that are localized and more or less chronic. *Prophylactic vaccination* has been employed successfully against smallpox (first known form of vaccination), typhoid fever, and rabies, and with encouraging results against cholera and plague. The protection afforded by active immunization is much more enduring than that afforded by passive immunization.

As a *means of cure*, vaccination has given satisfactory results in certain forms of localized tuberculosis, staphylococcus infections of the skin (furunculosis), chronic local streptococcus infections, and chronic gonorrheal infections. Owing to the existence of many strains of the same kind of bacteria, it is desirable to

employ an *autogenous vaccine*, that is one prepared from the lesion of the person to be treated. In some instances, however, this may be impossible, and then it is permissible to use a so-called *stock vaccine*, or one composed of organisms of the same kind as those found in the lesion to be treated but obtained from an infectious process in another individual. In acute, widely disseminated infections vaccination has not yielded satisfactory results. *A priori*, this might have been expected, for a pronounced toxemia being already present in such infections it would seem impossible to hasten the process of immunization by the artificial introduction of more toxin.

Passive Immunization.—Two types of sera are available for passive immunization: antitoxic and antibacterial. Antitoxic sera protect against the harmful effects of toxins, and are especially serviceable in diseases caused by organisms which have little power of becoming generalized, but which nevertheless may kill through their toxic properties. On the other hand, antibacterial sera should theoretically prove efficacious in diseases excited by organisms which have a high degree of aggressivity and rapidly become generalized, but which have little or no power to release soluble toxins. Practically, however, the value of antibacterial sera is very limited.

For prophylactic purposes, *antitoxic immunization* has been found to be especially valuable in the case of two infections: diphtheria and tetanus. The organisms of these diseases are active toxin producers, but as they have little aggressivity (power to multiply and become generalized), the tissues are usually capable of overcoming the infection, provided the toxins are prevented from doing harm.

The protection afforded by antitoxic sera is relatively brief, lasting only for a few weeks. As a curative measure antitoxic immunization has given the best results in diphtheria. In bacillary dysentery, cholera, tetanus, plague, and certain snake envenomations the results, although encouraging, have been less definite. *Antibacterial immune sera* have been used in a number of infections caused by pathogenic cocci, but in only two, meningococcus infection and Type I pneumococcus infection, have noteworthy curative results been achieved. Antibacterial immune sera have been employed also for prophylactic purposes in various infections, but in no instance has their usefulness been conclusively demonstrated.

Anaphylaxis.—It has long been recognized that the injection of foreign albumins (serums) is occasionally followed by toxic symptoms. This abnormal susceptibility is now known to be due to a condition of protein sensitization, or of what Richet has

termed anaphylaxis (absence of protection). In the majority of cases this peculiar supersensitiveness follows at intervals of from ten days to several weeks (in man the optimum period is from 1 to 6 months) a primary or "preparatory" injection of foreign serum (antigen), and the anaphylactic shock only occurs when a second or "exciting" dose of the same serum is injected. In some instances, however, the supersensitiveness appears to be congenital, for in certain individuals anaphylactic shock may be evoked by first injection of serum. Nearly all the fatal cases in man belong to this variety. The reaction is specific for each protein and may not disappear for years. The chief symptoms of anaphylactic shock are collapse from paralysis of the arterioles, intense dyspnea from spasm of the bronchioles, erythematous or urticarial rashes and in some cases, probably as results of the asphyxia, convulsions and coma. The symptoms develop quickly, often within a few minutes of the injection, and last only a few hours, the animal either rapidly recovering or dying. Important from a practical viewpoint is the discovery that if an animal is reinjected not later than ten days after a first injection, the reaction is slight or absent, and that subsequent injections for a period of several weeks give rise to no serious consequences (antianaphylaxis).

Fortunately, in human beings serious anaphylactic symptoms are uncommon; indeed, the danger is so slight in comparison to the advantages of serum treatment in certain diseases that it should not be regarded as a bar to a second or third dose of serum when the latter is clearly indicated. Serious reactions have been most frequently observed in persons who develop unpleasant symptoms, especially sneezing and dyspnea, when coming in contact with horses. A method of treatment sometimes adopted in cases in which anaphylactic shock is feared consists in a preliminary injection of a small quantity of serum (0.5 mil). After three hours, if no general reaction occurs, a full dose of the serum may be given. It has been shown that even administering the serum with extreme slowness may be sufficient to prevent anaphylactic shock in animals. The suggestion that sera for prophylactic purposes should be obtained from the ox, thus reserving horse serum for the treatment of diseases subsequently contracted seems to be a good one.

Anaphylactic shock is best treated by subcutaneous injections of atropin ($\frac{1}{100}$ grain—0.00065 gm.) and of epinephrin (1 mil of 1:1000 solution), and the practice of artificial respiration.

Serum Sickness.—This condition is really an anaphylactic phenomenon, but it is usually considered separately, because it is only a mild manifestation of hypersensitiveness to foreign protein.

It rarely appears until a week or ten days after the injection of serum and is characterized by urticarial or erythematous rashes, fever, and sometimes slight polyarthritides. The soluble salts of calcium by the mouth have some power to prevent it, and atropin hypodermically may afford some relief after it has actually developed.

SERUM ANTIDIPHThERICUM, U. S. P.

(Diphtheria Antitoxin)

Diphtheria antitoxin is obtained from the horse, the animal having been rendered artificially immune by repeated injections extending over a period of several months of gradually increasing quantities of the strongest diphtheria toxin. As the bacilli themselves are not injected, the horse does not become infected with diphtheria, but he gradually acquires a tolerance for the toxins of the disease and develops in his blood a substance (antitoxin) which has the power to neutralize those toxins. At the proper time, when it is thought that his blood has acquired the requisite degree of potency, the animal is bled, and the serum—the part of the blood containing the antitoxin—is carefully separated from the clot, filtered, and standardized. The last procedure is accomplished by determining the quantity of antitoxin serum required to offset the effects of the minimum quantity of toxin necessary to kill a guinea-pig in a definite time. The strength of the antitoxin is measured in units, a unit containing the amount of antitoxin required to save the life of a guinea-pig which has been injected with 100 fatal doses of toxin. Irrespective of the toxin injected and of the duration of the immunizing treatment, the serum yielded by different horses varies considerably in antitoxin strength. Only a very small percentage of horses give more than 1000 units in a cubic centimeter.

Concentrated serum, prepared by isolating the antitoxin globulins, is official as *Serum Antidiphthericum Purificatum*.

Therapeutics.—Diphtheria antitoxin has both prophylactic and curative power. *Passive immunization* affords protection for from 2 to 4 weeks. The dose is 500 units for infants under one year and 1000 units for older children. If time permits the Schick test should be made, as only those persons who yield positive reactions require the antitoxin. *Active immunization*, although more slowly developed than passive immunization, is much more enduring and is therefore preferable when time permits. The material employed for the purpose consists of a mixture of strong diphtheria toxin and antitoxin in such propor-

tions that the toxin is just neutralized or is in very slight excess when tested on a guinea-pig. Three injections of the mixture (T.-A.) are given subcutaneously at weekly intervals, the dose being 0.5 mil for infants under one year and 1 mil for older children and adults. According to Park, one injection gives immunity to 80 per cent. of persons previously susceptible, two injections, to 90 per cent. and three injections to 97 per cent. The immunity conferred lasts for at least 3 years and probably very much longer. Park has seen no serious untoward effects from the injections in 10,000 cases.

That antidiphtheria serum has remarkable curative power is evident from the fact that the mortality of diphtheria has been reduced at least two-thirds since the introduction of the antitoxin. Indeed, in private practice the mortality in cases treated on the first day of the disease is less than 4 per cent. The chances of recovery in all cases vary directly with the time of administration, the mortality steadily increasing from about 4 per cent. in cases treated on the first day to 20 per cent. or more in the cases treated on the fourth day. In cases of faucial or tonsillar diphtheria, which are of moderate severity and which are first seen on the second day of the disease, the initial dose should not be less than 10,000 units. If the patient is seen on the first day and the patch is small and confined to one tonsil, it should be not less than 5000 units. In laryngeal diphtheria the dose should be from 10,000 to 20,000 units, according to the time at which treatment is instituted. In well-marked nasal diphtheria, unless the patient is seen very early, the dose should not be less than 15,000 units. Age need only be considered in the case of young children under 2 years, and in them the dose should be about one-half that required for older persons. Unless there is a definite improvement, as shown by the appearance of the throat and the patient's general condition, the treatment should be repeated in 12 hours. In severe cases, if no improvement is observed, a second and larger dose should be given within six hours. In some cases it is necessary to administer three, four or more doses of antitoxin. The danger lies not in using too much, but in using too little.

Administration.—Except in malignant or profoundly toxic cases, when it may be given intravenously, antitoxin should be injected subcutaneously or intramuscularly, preferably in the pectoral region, abdominal wall, or flank. The injections should be made under aseptic precautions. Massage of the swelling to hasten the absorption of the serum is undesirable. When intravenous injections are employed, the serum should be heated to the body-temperature and introduced slowly, at a rate not

exceeding a mil per minute. Turbid serum should be discarded. The dose for intravenous injection is from one-half to two-thirds of that recommended for subcutaneous or intramuscular administration.

Untoward Effects.—*Serum sickness*, which is characterized by an urticarial or erythematous rash, with a slight rise of temperature, and, in some cases, with arthralgia and nausea, is not uncommon. *Anaphylactic shock* (see p. 464) may also occur, but fortunately, it is rare. Most of the fatal cases have been in persons in whom contact with horses has regularly caused asthma, paroxysmal sneezing or urticaria. According to Park, about one death has occurred for every 70,000 persons injected.

SERUM ANTITETANICUM

(Tetanus Antitoxin)

Tetanus antitoxin is prepared in the same manner as diphtheria antitoxin, that is, by immunizing horses with gradually increasing doses of tetanus toxin over a period of several months. The American unit is the amount of antitoxin required to neutralize exactly 1000 fatal doses of tetanus toxin for a 350-gram guinea-pig.

Therapeutics.—The value of tetanus antitoxin as a prophylactic remedy when it is used before the tetanus toxin has become fixed to the cells of the spinal cord has been amply demonstrated. Although it is not invariably successful in preventing the disease, when used early and in sufficient amount, it decidedly lessens the likelihood of infection, and if the latter does occur, tends to mitigate the violence of the attack. During the World War the incidence of tetanus in the British Army was apparently reduced by universal immunization from 32 per thousand to 2 per thousand. It is particularly important to employ tetanus antitoxin as a prophylactic remedy in the case of wounds contaminated with stable refuse, garden earth, or street dirt, gunshot wounds and those made by blank cartridges, toy pistols or fire crackers, punctured wounds made by iron nails, large splinters, pitch forks, etc., and all severe crushing injuries. The immunizing dose is 1000 units for an adult or 500 units for a child. Multiple injections at weekly intervals are often required because the protective power of the serum does not usually endure longer than a week or ten days and the incubation period of tetanus is not infrequently several weeks.

The curative power of tetanus antitoxin is much less certain than its usefulness as a prophylactic measure. The chief reason for this is that the diagnosis of tetanus cannot be made until the

toxin has entered into firm union with the sensitive receptors in the central nervous system, which are for the most part inaccessible to the antitoxin. Nevertheless, most observers believe serum is of value when it is used promptly and in large doses. It is best administered intrathecally and subcutaneously or intramuscularly. Intravenous injection has had its advocates, but it has largely been discarded on account of the risk of anaphylaxis. Intraneural administration is also recommended, and is a rational procedure, especially when localized rigidity is an early sign. At least 3000 units should be given intrathecally, after removal of a requisite amount of cerebrospinal fluid, and the treatment should be repeated daily for four or five days. At the same time from 10,000 to 25,000 units should be administered intramuscularly or subcutaneously, and, unless improvement occurs and is sustained, a similar amount should be injected again in from 18 to 24 hours. The drawback to subcutaneous and intramuscular injections is the extreme slowness of absorption. In the case of ascending tetanus from 500 to 1500 units may be injected into the main nerve trunk.

ANTIMENINGOCOCCUS SERUM

Antimeningococcus serum is prepared by immunizing horses with different strains of meningococci. The injections are given every few days, in increasing doses and for a period of several months, or until a high degree of immunity is attained. The chief action of the serum is bactericidal, although it also possesses some antitoxic power. Since the use of the specific serum in the treatment of epidemic meningitis the mortality of the disease has been reduced about one-half, or from 70 to 75 per cent. to 30 to 35 per cent. When given before the third day, the death-rate apparently does not exceed 15 to 20 per cent. Only polyvalent serum standardized against all representative strains of meningococci should be employed.

As a rule, antimeningococcus serum should be administered by intraspinal injection. The dose for adults is from 30 to 50 mls, and for infants and children from 5 to 20 mls, the amount varying with the quantity of cerebrospinal fluid withdrawn. In children, especially, the dose should be a few mls less than the amount of fluid removed. When only a small quantity of cerebrospinal fluid is obtained, not more than 10 mls of serum should be injected. In cases of moderate severity the injections should be given every day, for 3 or 4 days, and then every other day until the patient's general condition and the result of the examination of the cerebrospinal fluid indicate that the infection

has subsided. If the case is severe and not seen until after the third day, the first injections should be given every 12 hours. The average case requires in all from 4 to 8 injections. The serum should be introduced slowly and preferably by the gravity method. If symptoms of collapse appear some of the fluid should be allowed to escape through the needle.

When the patient is seen early and bacteriemia can be demonstrated serum may be given also intravenously, although with this method of administration there is likely to be a severe systemic reaction, especially in children. The dose of serum for intravenous injection is from 30 to 120 mils, daily for several days, the amount varying with the age of the patient and the severity of the attack. The injection should always be made very slowly and to avoid serious reactions, it is advisable to desensitize the patient first by giving an hour before the intravenous injection 1 mil of the serum subcutaneously.

Intraventricular injections of the serum have sometimes proved efficacious when persistence of symptoms and failure to obtain fluid by lumbar puncture have indicated the occurrence of acute hydrocephalus. The dose for an adult is 30 to 70 mils, according to the amount of cerebrospinal fluid withdrawn. The serum is introduced once in 24 hours through a trephine opening or the open fontanel.

ANTIPNEUMOCOCCUS SERUM

It has been proved conclusively that the serum of horses immunized by repeated injections, first with dead and then with living cultures, of Type I pneumococci is of great value in the treatment of pneumonia due to Type I pneumococci. This serum, however, is not effective against other forms of pneumococcus pneumonia, and according to Flexner, no scientific basis exists for the manufacture or the administration of a so-called "polyvalent" antipneumococcic serum. The mortality in cases of pneumonia due to Type I pneumococcus, which constitute about one-third of all cases of pneumonia, has apparently been reduced by serum therapy from 25 to 30 per cent. to about 10 per cent. The serum possesses both bactericidal and antitoxic properties.

The dose of the antiserum is from 90 to 100 mils, repeated every 8 hours until a fall of temperature and an improvement in the other symptoms of the disease indicate that the infection has been overcome. The total amount required in an average case is from 200 to 300 mils. To secure the best results the serum should be given as early as possible and intravenously. In young

children intramuscular injections may be substituted. To avoid serious anaphylactic reactions the patient should first be desensitized by the administration of a small amount of serum (1 mil) subcutaneously an hour or two before the intravenous injection is given, and under all circumstances the serum should be introduced into the vein very slowly.

The intravenous injection of a serum-free solution of antibodies of the three fixed types of pneumococci, prepared after the method of Huntoon, has given encouraging results in some series of cases of pneumonia, although it is followed by a severe, and sometimes a dangerous, thermal reaction. Anaphylactic phenomena, however, are never produced by the treatment. The preparation of the solution is based upon the capacity of bacteria to absorb their specific antibodies from immune serum. The pneumococci, after being exposed to the action of a polyvalent immune serum, are separated from the serum proteins by centrifugation and washing, and then treated with a mildly alkaline salt solution in which some of the attached antibodies split off. The injections are begun as soon as the diagnosis is established and are repeated daily, the dose for a man being about 50 mls and for a woman 25 mls.

ANTIPOLIOMYELITIC SERUM

The blood serum of persons who have recently passed through attacks of acute poliomyelitis has been employed with encouraging results in the treatment of this disease. During epidemics antiserum may be obtained from different individuals and "pooled." The treatment is carried out by intraspinal injections, or preferably by intraspinal and intravenous or intramuscular injections. The amount of serum injected intraspinally varies with the amount of cerebrospinal fluid withdrawn. The usual dose for a child is from 10 to 20 mls. For intravenous or intramuscular injection the dose is from 40 to 100 mls, according to the age of the child. It is advisable to repeat both the intraspinal and the intravenous injections in 24 hours if the temperature still remains above normal.

ANTIANTHRAX SERUM

Selavo and others have prepared an antianthrax serum which is apparently effective both as a prophylactic and as a therapeutic agent, in cattle as well as in man. The serum owes its activity to opsonins and bacteriolysin. It is prepared by immunizing sheep, asses and horses with virulent cultures of anthrax bacilli. In 164 cases in Italians treated by Selavo with serum the mortality

was only 6 per cent., in contrast to 24 per cent., the rate of all cases treated in Italy over a period of 15 years (Legge). The serum should be given intramuscularly or intravenously, in doses of 50 to 100 mils, and repeated in 24 hours, if there is no improvement.

ANTIDYSENTERY SERUM

Serum prepared by injecting horses with cultures of the Shiga bacillus neutralizes both the exotoxin and the endotoxin of this organism and protects against infection with living bacilli. It is, however, highly specific and is of no value either in the prophylaxis or the treatment of dysentery caused by the Flexner group of bacilli, which is the prevailing form of the disease in the United States. An antiserum is also prepared in the usual way for neutralizing the only toxin (endotoxin) produced by the Flexner bacilli and for protecting against infection with these organisms. This serum is also specific.

A mixture of the two serums constitutes so-called polyvalent antidyentery serum and this should be used in cases of bacillary dysentery when it is not definitely known whether the infection is due to the Shiga or the Flexner group of bacilli.

Serum treatment has apparently reduced the mortality of *acute bacillary dysentery* from 50 to 75 per cent. In chronic cases the results have been disappointing. Infantile diarrheas caused by dysentery bacilli are also refractory to serum treatment. Antidyentery serum is usually given subcutaneously, the dose for an adult ranging from 10 to 100 mils, according to the severity of the attack. The average dose for a child is 10 mils. In very severe cases in adults from 50 to 100 mils may be given intravenously. The treatment should be repeated, if necessary, in from 12 to 36 hours.

Polyvalent serum has also protective power, and has been employed with encouraging results in combating outbreaks of dysentery in institutions, camps, etc. The usual prophylactic dose is from 5 to 15 mils subcutaneously. It is often necessary to repeat the injections as the protection lasts only about two weeks.

ANTISTREPTOCOCCUS SERUM AND STREPTOCOCCUS VACCINES

A serum obtained from horses after they have received repeated injections of streptococcus cultures (usually several strains) has been employed as a remedy in various diseases resulting from streptococcus infection. These diseases include erysipelas, scarlet fever, puerperal septicemia, phlegmonous cellulitis,

empyema, and ulcerative endocarditis. Numerous cases are on record in which good results are attributed to the serum, but statistics collectively do not indicate that it has had any very decided influence in lowering the mortality of septic diseases. Whatever value the serum has depends chiefly upon bacteriotropins or specific opsonins. The serum should be polyvalent, should be used as early in the disease as possible, and should be given in large doses—50 mils intravenously or 100 mils intramuscularly. The treatment should be repeated, if necessary.

Streptococcus Vaccines.—In protracted streptococcus infection, especially if the process is one in which there is no obstruction to drainage, autogenous streptococcus vaccines are sometimes very efficacious. Polyvalent stock vaccines, owing to the many strains of streptococci, are rarely of service. In acute generalized streptococcus infections vaccines are contraindicated. Streptococcus vaccines should be administered subcutaneously, at intervals of about three days, in increasing doses, the initial dose containing from 15 to 20 million bacteria.

ANTISTAPHYLOCOCCUS SERUM AND STAPHYLOCOCCUS VACCINES

Serum prepared by immunizing animals with different strains of staphylococci has been used to some extent in the treatment of infections due to staphylococci, but without much success. *Vaccines* of staphylococci, however, sometimes prove very useful in localized infections due to these organisms, especially furunculosis and sycosis vulgaris. Good results have also been reported from the use of a mixed vaccine of staphylococcus and acne bacillus and of these two organisms with *Bacillus coli communis* in acne vulgaris (Strickler, Schamberg and Kolmer).

ANTITUBERCULOUS SERUM AND TUBERCULINS

Maragliano and Marmorek have prepared *antituberculous serums*, which have been used somewhat extensively, but not with very encouraging results. Maragliano's serum is prepared by immunizing horses over a period of several months with a mixture of the filtrated young cultures of tubercle bacilli and aqueous extract of killed virulent cultures. This serum is said to be both bactericidal and antitoxic. Marmorek's serum is prepared by immunizing horses first with young tubercle bacilli and later with various strains of streptococci and is therefore antituberculous and antistreptococcic.

Tuberculins.—In 1890 Koch introduced as a specific remedy for tuberculosis a preparation to which the name *tuberculin* was

applied. This was subsequently shown to be an extract of the metabolic products of tubercle bacilli preserved in glycerin.

Koch did not consider this original tuberculin as an immunizing agent, but believed that by reinforcing the toxin already in the body it would increase the irritation at the site of infection, attract leukocytes, and, ultimately, lead to the complete encapsulation of the bacilli. It is now known, however, that Koch's tuberculin and all similar preparations are in reality vaccines, which may do good in tuberculosis by stimulating the defensive resources of the organism. Unfortunately, tuberculin at first was applied without skill and often in unsuitable cases, and, consequently, it soon fell into discredit. During the last two decades it has again been employed, especially in sanatoriums, and has gained the reputation of being of definite, but limited, value, when used in appropriate doses and in certain phases of the disease. Originally, it was supposed that definite reactions on the part of the patient were a necessary consequence of the treatment, but at present it is recognized that such reactions are essentially harmful. The cases best adapted to tuberculin treatment are those in which the general nutrition is good and the fever is slight.

Many preparations of tuberculin are in use, but it is doubtful if any one has any special advantage over another. The most important preparations are: Koch's Old Tuberculin, O.T.; Koch's Tuberculin Rest, T.R. (the residue obtained by centrifugalizing finely pulverized virulent cultures of tubercle bacilli suspended in distilled water); Koch's New Tuberculin or Bacillen Emulsion, B. E. (an aqueous emulsion of finely pulverized virulent bacilli preserved by the addition of glycerin); and Deny's Broth Filtrate, B.F. (similar to Koch's original tuberculin). No matter which tuberculin is selected, the initial dose should be very small— $\frac{1}{10,000}$ milligram of Old Tuberculin, of Tuberculin Rest, of Broth Filtrate, or $\frac{1}{100,000}$ milligram of Bacillen Emulsion. The injections should be given at first at intervals of 3 to 7 days, the dose being gradually increased, but never large enough to cause a reaction, not even a slight rise of temperature. The maximum dose varies with the individual. With Old Tuberculin it may be as high as 1000 milligrams or as low as a few hundredths of a milligram. Of Tuberculin Rest (T.R.) the final dose may reach 10 milligrams or more, of the Bacillen Emulsion (B.E.) the final dose is 5 milligrams (solid substance), and of Deny's Broth Filtrate (B.F.) the usual maximum dose is 20 milligrams. When $\frac{1}{100}$ milligrams is reached the interval should be at least a week and the largest doses should be given only at intervals of 2 or 3 weeks. If evidences of increasing sensitiveness appear, the injections should be stopped for a time and then resumed

with smaller doses. The treatment is not likely to be of permanent value unless faithfully followed for at least 4 or 5 months.

The contraindications to tuberculin treatment are rapid emaciation, high evening temperature, a pulse-rate persistently above 100, pregnancy, diabetes, nephritis, and active pleurisy. Hemoptysis and intercurrent infections call for suspension of the injections for a time.

ANTITYPHOID SERUM AND TYPHOID VACCINE

As no specific soluble toxin has been isolated from cultures of typhoid bacilli, it has been impossible to prepare an *antitoxin serum* for typhoid fever, as has been done for diphtheria, although Chantemesse claims to have reduced the mortality of typhoid fever in Paris from 17 per cent. to 4.3 per cent. by using a serum obtained by inoculating horses with filtrates of *B. typhosus* in bouillon containing spleen pulp and defibrinated human blood.

Typhoid Vaccine.—The injection of killed preparations of the typhoid bacillus at intervals of a few days (100 million increased to 500 million) has been employed to some extent in the treatment of typhoid fever, but the results have been equivocal. On the other hand, antityphoid vaccination as a prophylactic measure has yielded brilliant results. For the purpose, combined vaccines prepared from heat-killed typhoid bacilli and alpha and beta paratyphoid bacilli are preferable, the typhoid bacillus comprising 50 per cent. of the organisms in suspension. The initial dose is one billion and the later doses are each two billion bacteria. At least three inoculations should be given spaced about one week apart. The inoculations are made subcutaneously (not intramuscularly) over the insertion of the deltoid muscle, after the site has been painted with tincture of iodine. Most persons experience both a local and a general reaction, the last, which is never serious, consisting of headache, malaise, fever, muscular soreness, and occasionally nausea, vomiting or diarrhea. After being inoculated, the person should rest for twenty-four hours. The duration of the immunity afforded by vaccination is from 2 to 3 years. The value of antityphoid vaccination is clearly shown in the United States Army reports. Thus, in the period between 1909 to 1914 there was only 1 death from typhoid in the army (80,000 men), while the average death-rate for the same period in the country at large was over 16.5 per hundred thousand. During the European War the reports were equally favorable. Whether antityphoid vaccination is ever universally adopted or not, its employment should be urged in the case of soldiers, sailors, physicians,

nurses, hospital orderlies and others who are in special danger of contracting the disease.

ANTICHOLERA SERUM AND CHOLERA VACCINES

It has been shown by Pfeiffer and others that the blood-serum of human beings who have recently recovered from attacks of cholera and of animals which have been artificially immunized has the property of disintegrating and dissolving cholera vibrios. Unfortunately, antiserum has thus far proved unavailing when applied to the treatment of cholera in human beings. Haffkine and Kolle, however, have been measurably successful in producing active immunity in human beings by subcutaneous injections of *vaccines*. Haffkine uses living cultures, injecting first vibrios of feeble virulence and later virulent vibrios. Kolle employs heat-killed cultures. According to Murata, in a certain district of Japan, of 825,287 non-vaccinated persons 1152 contracted the disease and 863 died, while of 77,907 vaccinated (Kolle's vaccine) persons only 48 were attacked and 20 died.

ANTIPLAGUE SERUM

In 1895 Yersin demonstrated that animals could be successfully immunized against bubonic plague by subcutaneous injections of sterile cultures of plague bacilli, and further that the blood-serum of animals thus artificially immunized possessed protective and curative properties. Serum obtained after the method of Yersin has been used with asserted good results in Canton, Amoy, Annam, Oporto, and elsewhere, but the report of the Plague Commission of India (1913) was not especially favorable to the treatment. The serum is best given by intravenous or intramuscular injection at intervals of 12 to 24 hours for several days. The dose is from 50 to 150 mils.

RABIES VACCINE

To Pasteur belongs the credit for having first demonstrated that full protection against rabies may be afforded by subcutaneous injections of suitably attenuated virus. Virus that has been passed through a series of rabbits (*virus fixé*) produces the disease more quickly, but in a much milder form than natural virus, and when subjected to desiccation by suspension over caustic soda becomes still further attenuated. The plan of treatment consists in inoculating the patient on successive days with virus of increasing virulence, the material for the purpose being obtained from the spinal cords of rabbits which have been artificially infected. The prepared cord is designated one,

two, three day cord, etc., according to the degree of desiccation to which it has been subjected. A piece of dried cord equivalent to 1 cm. of fresh cord, freed of preservative glycerin, and thoroughly emulsified in 2.5 mls of sterile saline solution is the uniform dose. The injections are given into the subcutaneous tissue of the abdominal wall, after the site has been painted with tincture of iodine. With the vaccine prepared by the U. S. P. H. S., the course of treatment consists of 25 injections which are given over a period of 21 days. The treatment is relatively harmless, although in rare instances it is followed by paralysis (occasionally fatal), the cause of which is not definitely known. The report of the Pasteur Institute of Paris shows that since its foundation the mortality from rabies has been but 0.5 per cent., whereas before vaccination was employed 5 per cent. of those bitten were attacked by rabies and all who were attacked died.

NON-SPECIFIC PROTEIN THERAPY

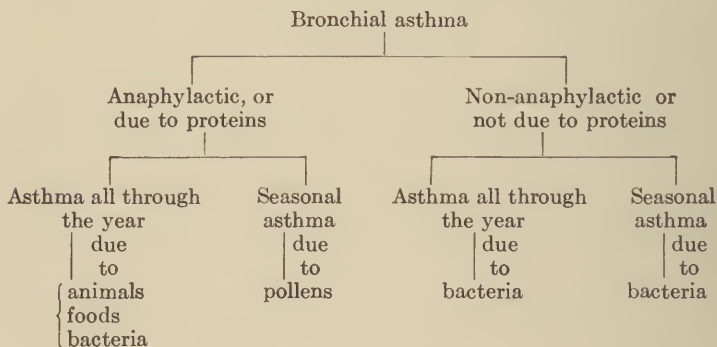
Good results have been reported by many investigators from the intravenous injection of foreign protein in various infectious diseases, including the arthritides, typhoid fever, pneumonia, puerperal sepsis, gonorrheal complications, and anthrax. Bacterial protein, especially typhoid vaccine, has been most frequently employed, but other vaccines, horse serum, beef serum and albumose solutions have also been used to a greater or less extent. The injection almost always produces a definite reaction characterized by chill, fever, sweating and leukopenia, followed by a pronounced polymorphonuclear leukocytosis. In localized infections, such as arthritis, a temporary aggravation of the symptoms may also occur and in certain febrile conditions, such as typhoid and pneumonia, crisis or rapid lysis may be initiated. The effects of the injections have been variously ascribed to activation of the leukocytes, increased production of antibodies, mobilization of enzymes, stimulation of the ductless glands, etc., but a satisfactory explanation is still lacking.

Typhoid vaccine is prepared in the usual way, killed by heating to 55° C. (131° F.), and preserved by 0.5 phenol. The dose varies from 75 million to 200 million bacteria, and the injections are given once a day or once every other day. If any benefit is to be secured from the treatment, from 1 to 3 injections will suffice in such diseases as typhoid fever, pneumonia and puerperal sepsis, but in the arthritides as many as 10 injections may be required. The foreign protein is apparently harmless when the dose is no larger than is necessary to excite a chill. Cardiac insufficiency is a contraindication.

Reports upon non-specific protein therapy have not been uniformly favorable in any disease, but are sufficiently encouraging to warrant a further trial of it in certain infections. In acute and subacute infective arthritis this method of treatment has given good results in many instances, but in the chronic forms of the disease it has usually failed. In pneumonia of the pneumococcus and influenzal types a crisis has occasionally followed the first injection. In typhoid fever a crisis or rapid lysis may occur after the second or third injection. Kraus and Penna report but one death in 146 cases of human anthrax in man treated with normal beef serum (30–50 mils subcutaneously or intravenously), but other reports have been less favorable. In septic endocarditis the results have not been favorable.

FOREIGN PROTEINS AND VACCINES IN THE TREATMENT OF BRONCHIAL ASTHMA

Bronchial asthma has been classified into two types: The anaphylactic and the non-anaphylactic. The following scheme suggested by Walker serves as a good working basis:



The type may usually be determined from the age of the patient, the history, and the results of skin tests with various proteins. Asthma after the age of 40 is rarely anaphylactic, but is virtually always infectious and due to bacteria present in the respiratory passages themselves or in such foci as are frequently found in the teeth, tonsils, nasal accessory sinuses, etc. Asthma following pertussis, measles, or persistent catarrhal affections of the upper respiratory tract is also commonly due to bacteria, but in this case either the protein element of the bacteria or the infectious element may be the important factor, and to solve the problem recourse may be had to skin tests. Asthma occurring in the first two or three years of life is, as a rule, anaphylactic and

due to food, especially milk, eggs, wheat or other cereals. Asthma appearing in childhood or early adult life may be caused by plant pollens, animal emanations or bacteria. Seasonal asthma is often, but not always, anaphylactic. The pollen of ragweed or golden rod is the chief cause of the anaphylactic type occurring in the late summer and continuing until frost; and the pollen of red top or timothy, of the anaphylactic type that appears only during June and July. Of the animals, the horse plays the chief rôle in the etiology of asthma, although the cat is not rarely a factor. In the case of the horse the sensitization may be to the dandruff or to the serum.

A complete list of proteins ready for use as test substances are now available and a number of them may be tested at one time. After cleansing the forearm with soap and water and thoroughly drying the skin, several discrete abrasions are made through the epidermis with a sharp scalpel. A drop of tenth normal sodium hydroxid solution and a minute quantity of the dry protein are then placed on an abrasion with a wooden applicator and are well mixed. This process is repeated with the different proteins, a new applicator being used for each protein. At the end of a half hour the proteins are washed off and the results compared with a normal control, that is, with an abrasion which has been treated only with the sodium hydroxid. A positive reaction consists of an urticarial wheal, about 0.5 cm. in diameter, surrounded by a pronounced erythematous areola. It is not usually necessary to test a great number of proteins, for, as Walker has shown, the majority of patients with anaphylactic asthma are sensitized to the proteins of the pollens, horse dandruff, wheat or other cereal flours, staphylococcus pyogenes aureus, staphylococcus pyogenes albus, cat hair or egg. A few patients are sensitive to the protein of milk, feathers, chicken meat, beef, potato, or wool.

The specific treatment of bronchial asthma varies, of course, with the cause of the disease. Excellent results are sometimes obtained in anaphylactic asthma due to pollens from the subcutaneous administration of dilute solutions of an extract of the particular pollen that is responsible for the attacks. The best method is to begin the treatment three months before the time of pollination, giving at first a dilution less than that capable of exciting a cutaneous reaction, and gradually increasing the dose until it reaches a few tenths of 1 mil of 1:100 extract. The injections are made at weekly intervals, so that 12 doses in all are given. Treatment that is begun during the time of pollination, although sometimes successful, is, on the whole, much less satisfactory, and unless carried out very cautiously may aggra-

vate the symptoms of the disease. Asthmatics sensitized to animal emanations frequently become desensitized for long periods by repeated injections of the offending protein in gradually increasing doses. Asthma caused by sensitization of the patient to food proteins is rarely amenable to desensitizing treatment, and is best controlled by eliminating from the diet the particular food the protein of which gives a positive skin reaction. The infectious forms of asthma are sometimes successfully treated by removing the focus of infection, if possible, and administering vaccines prepared from cultures of the offending organism.

ANTIVENINS

The studies of Sewall, Phisalix, Bertrand, Calmette and others have established the fact that animals can be successfully immunized against the venom of certain snakes by being inoculated with increasing doses of venom, and, further, that the blood-serum of animals thus treated possesses both protective and antidotal properties. The more recent work of Noguchi, Flexner and others has shown, however, that antivenins are highly specific and that a preparation which is effective against the venom of one species of reptile is useless in the envenomation of another species. Calmette has produced a satisfactory antiserum for cobra neurotoxin and Noguchi has produced an antiserum which neutralizes the hemorrhagin of *Crotalus* venom. Thus far, antibodies have not been successfully produced against the locally destructive poisons of the rattlesnake, copper-head or moccasin.

YEAST

Yeast has some power to combat infection, especially staphylococci, and probably acts by promoting leukocytosis. It has given the best results in recurring furunculosis. It has been used with some success also in intestinal indigestion with constipation. The dose is from $\frac{1}{3}$ to $\frac{1}{2}$ of a compressed yeast cake in a tumblerful of water, two or three times a day, with meals. The treatment may be continued, if necessary, for several weeks.

IRRITANTS AND COUNTERIRRITANTS

Irritants are agents which, when applied to the surface of the body, cause active hyperemia or inflammation. When they are applied not simply for their local action, but to influence for the better adjacent or remote morbid processes, they are termed **counterirritants**. We have yet no clear understanding

of the manner in which counterirritants do good; the most plausible theory, however, is that they call forth reflexly from the central nervous system centrifugal influences, vasomotor or trophic or both, which act favorably upon local disturbances.

Counterirritants which produce merely an acute hyperemia of the skin are known as *rubefaciens*; those which act more severely and lead to the formation of blisters are termed *vesicants* or *epispastics*; and those which act especially on the ducts of the sudoriferous glands, producing a crop of pustules, are called *pustulants*.

Counterirritation may be carried to a still greater degree of intensity by producing ulceration, and for this purpose it is now customary to use the *actual cautery*. This may be applied by means of irons of various shapes, heated to whiteness, or, better still, by means of the Paquelin cautery, in which heated platinum-sponge is brought to full incandescence by contact with the vapor of naphtha or rhigolene.

Light applications of the thermocautery are often efficacious in certain deep-seated affections attended with severe pain, such as sciatica, chronic meningitis, arthritis, and locomotor ataxia.

Still another method of producing a counterirritant effect, applicable to certain painful affections, is *acupuncture*, which consists in thrusting fine needles deeply into the tissues. In sciatica and lumbago this treatment sometimes gives excellent results. The needles should be 4 or 5 in. long and about the thickness of a bonnet-pin. Having been sterilized, they should be inserted into the most painful spots to a depth of 2 or 3 in., and allowed to remain for from 10 to 15 minutes.

The most important *rubefaciens* are:

Mustard	Capsicum
Iodin	Chloroform
Oil of turpentine	Ammonia
Arnica	Camphor
Pitch	Volatile oils.

Rubefaciens may be applied with advantage in acute congestion of the internal organs, in inflammatory affections of a mild type, and in neuralgic pains. Thus, they are useful in acute congestion of the lung, acute bronchitis, acute catarrhal enteritis, gastralgia, intestinal colic, myalgia, and neuralgia of the superficial nerves. When applied over large surfaces, they serve also as general stimulants, and as such may be employed to arouse the system in collapse, shock, and narcotic poisoning. They may be applied in the form of plasters (mustard), stupes (oil of turpentine), liniments (chloroform, arnica), or paints (iodin).

Other agents that are employed to produce mild counterirritant effects are *heat* (hot-water bottle, poultice, electric pad, stupe, etc.), *dry cupping* (see p. 544), and *constricting bands*, as in Bier's hyperemic treatment (see p. 547).

The chief *vesicant* is cantharides.

A number of the drugs classed as rubefacients (ammonia, mustard, chloroform, iodine), if applied in concentrated form, will also produce vesication, but they are never employed for that purpose.

Vesicants exert a more profound and a more lasting effect than rubefacients. They are often of service in inflammatory diseases of a severe type, such as pleurisy, pericarditis, gastritis, iritis, arthritis, neuritis, etc., and in refractory forms of neuralgia.

Vesicants are usually applied directly over the affected part, though some authorities hold that they should be placed some little distance from it. In neuralgia they are often most beneficial, as Anstie pointed out, when applied to a posterior branch of the spinal nerve-trunk from which the painful nerve issues. In trifacial neuralgia it is customary to apply the blister behind the ear.

Croton oil and tartar emetic (antimony and potassium tartrate) are *pustulants*, but are rarely used as such at the present time. However, a mixture of croton oil (see p. 223) and olive oil (1 to 3), or the liniment of croton oil of the British Pharmacopœia (croton oil, 1 part; cajuput oil and rectified spirit, of each, 3½ parts), is sometimes of benefit as a counterirritant in bronchitis, pleurodynia, and dry pleurisy.

Irritants.—A large number of drugs that produce irritation when applied locally are used for their stimulant effects upon the superficial tissues themselves in various forms of chronic inflammation, such as subcutaneous indurations, indolent ulcers, and certain chronic skin diseases. Only those, however, which are used almost exclusively for this purpose will be considered here:

Chrysarobin
Oil of cade
Jequirity

Chaulmoogra oil
Gurjun balsam
Scarlet red.

CANTHARIS, U. S. P.

(Cantharides, Spanish Flies)

Spanish fly is the dried beetle, *Cantharis vesicatoria*, secured chiefly in southern Europe. The active principle is *cantharidin*, an anhydrid of cantharidic acid. The latter does not exist

uncombined, but its salts are obtained by acting on cantharidin with alkalis. Cantharidin occurs in colorless prisms, readily soluble in alcohol, ether, chloroform, or oils, but only sparingly soluble in water.

PREPARATIONS

DOSE

Tinctura Cantharidis, U. S. P. 1 to 3 min. (0.06–0.2 mil)
 Ceratum Cantharidis, U. S. P. (cantharides, 35; yellow wax, 17.5; rosin, 17.5; benzoinated lard, 20; glacial acetic acid, 2.5; oil of turpentine, 15)
 Collodium cantharidatum, U. S. P. (cantharidal collodion: 60 per cent. of cantharides).

Pharmacologic Action.—When applied to the skin, preparations of cantharides produce redness and burning, and, later, vesication. If the action of the drug be allowed to continue, it may ultimately lead to pustulation, ulceration, and sloughing. A cerate of good quality requires from 6 to 10 hours to produce a blister, the time varying with the part to which it is applied and the condition of the skin. To mucous membranes, cantharides is also highly irritating, that of the urinary tract being especially susceptible to its influence.

Internally, doses of from 5 to 10 minims (0.3–0.6 mil) increase to some extent the excretion of urine, and often cause frequent desire to micturate, with some dysuria. The active principle of the drug is rapidly eliminated by the kidneys. Toxic doses are followed by intense irritation of the alimentary canal and of the genito-urinary tract. The symptoms of poisoning are burning pain in the mouth, throat and stomach, dysphagia, great thirst, ptyalism, vomiting and purging of mucous and bloody material, and extreme prostration. Later, when a sufficient quantity of the poison has been absorbed, symptoms referable to the genito-urinary tract appear, such as aching pains in the loins, a constant desire to urinate, severe vesical tenesmus, with the passage of merely a few drops of bloody, albuminous urine, and, in males, priapism. Erotic excitement sometimes occurs, and in women abortion may follow the powerful irritant effects of the drug upon the pelvic viscera. In fatal cases death may be preceded by coma and convulsions. If the cantharides has been taken in the form of powder, the characteristic shining green parts of the insect may be recognized in the vomitus. Section after death shows gastro-enteritis and glomerulonephritis.

Cantharides is absorbed readily from the skin, and a number of cases are on record in which severe and even fatal nephritis has resulted from too free vesication. Owing to unusual susceptibility, the use even of very small blisters in some persons is followed by strangury.

Treatment of Poisoning.—This consists in evacuating the stomach, and in relieving the local irritation by the free administration of demulcents. Opium may be required for the pain. Fatty substances should be withheld, as they dissolve cantharidin and so favor its absorption. The treatment of cantharidal nephritis does not differ from that usually adopted in other forms of the disease. The treatment of strangury consists in applying hot fomentations to the lower part of the abdomen, in giving freely diluent drinks, and in administering opium.

Therapeutics.—The most important use of cantharides is as a counterirritant. As a vesicant, it is often of decided value in acute inflammation of serous membranes—*pleurisy*, *pericarditis*, *synovitis*, etc. In the early stage of these diseases it tends to relieve the pain, and, later, it aids in the absorption of the effusion. In severe forms of *neuritis* small blisters may be applied with advantage over the course of the affected nerve. In *facial neuralgia* blistering behind the ear may afford speedy relief. In *acute rheumatism* the application of blisters around the inflamed joint will often relieve the pain and reduce the swelling. In *pneumonia* of the usual type blisters are useless or actually harmful, but they are sometimes efficacious when used repeatedly in cases of *delayed resolution*.

In the early stages of *pulmonary tuberculosis*, when the cough is troublesome, mild counterirritation with cantharides may prove beneficial. In *oöphoritis* the application of a blister over the affected gland is advantageous. *Obstinate vomiting*, due to acute irritation of the stomach, sometimes yields promptly to a vesicant applied to the epigastrium.

The tincture of cantharides, well diluted, has an established reputation as a stimulant lotion in the treatment of *premature alopecia* and *alopecia areata*.

R. Tincturæ cantharidis..... f ʒss (15.0 mils)
 Tincturæ capsici..... f ʒj (30.0 mils)
 Olei ricini..... f ʒss (2.0 mils)
 Alcoholis..... q. s. ad f ʒiv (120.0 mils).—M.
 Sig.—Rub into the scalp each night.

Internally, cantharides has been used to some extent as a stimulant to the genito-urinary tract, in *incontinence of urine from atony of the bladder*, and in *chronic pyelitis*, *cystitis*, and *urethritis*, but it is neither as safe nor as efficacious as many other remedies in common use. In large doses, probably by irritating the urethra, cantharides, sometimes excites the sexual appetite, hence it has been employed as an aphrodisiac; for this

purpose, however, it has no merit and is distinctly dangerous, owing to the tendency of the drug to cause nephritis.

Administration.—The tincture is the only form in which the drug is used internally. It should be taken after meals, well diluted. For blistering it is customary to use a plaster made of the cerate. The market is well supplied with good ready-made plasters, which may be cut the desired size and shape. To obtain the best results, the skin should be washed, and shaved if necessary, and then thoroughly dried; before the plaster is applied it should be moistened with vinegar. Vesication is generally induced in from 6 to 10 hours; even if it is not, it is advisable to remove the plaster at the end of that time and to complete the operation by applying a poultice. In delicate subjects the poultice should be used at the end of 3 or 4 hours. When the bleb has fully developed, it should be opened with a large needle, and then dressed with a pledget of dry cotton. In many cases excellent results are obtained from a succession of blisters applied to different parts of the affected region and allowed to remain only long enough to produce a rubefacient effect (*flying blisters*). Cantharidal collodion may be used as a blistering agent in cases in which there is difficulty in controlling the patient.

Contraindications.—Vesicants must be used with the greatest caution in very young, old, or debilitated subjects, as they may occasion sloughing. For the same reason they should be avoided in patients with diabetes. When there is active nephritis some other irritant than cantharides should be selected.

SINAPIS ALBA, U. S. P., AND SINAPIS NIGRA, U. S. P.

(White Mustard and Black Mustard)

White mustard is the seed of *Sinapis alba*, and black mustard is the seed of *Brassica nigra*. Both of these herbs are largely cultivated in Europe and America. The *mustard* sold as a condiment is a mixture of powdered white and black mustard, sometimes more or less adulterated.

White mustard contains a ferment, *myrosin*, and a glucosid, *sinalbin*. In the presence of water the ferment acts upon the glucosid and separates from it an acrid oil—*acrinyl iso-thiocyanate*. Black mustard also contains myrosin, and this ferment in the presence of water acts upon a glucosid, *sinigrin*, separating from it an intensely irritant and highly volatile oil—*allyl iso-thiocyanate*. Mustard seed also contains a large amount of bland fixed oil.

PREPARATIONS

Emplastrum Sinapis, U. S. P. (mustard plaster: Paper, cotton cloth or other fabric spread with a mixture of powdered black mustard and a solution of rubber).

Oleum Sinapis Volatile, U. S. P. (produced synthetically or obtained from black mustard).

Pharmacologic Action and Therapeutics.—Mustard made into a paste with water and applied to the skin causes redness, heat, and burning pain, and, if the contact be prolonged, vesication. As the blisters produced by mustard are healed with difficulty, the drug is used externally only as a rubefacient. Applied in the form of a plaster (*sinapism*), it often affords much relief in various painful affections, such as *bronchitis*, *cerebral congestion*, *headache*, *intestinal colic*, *gastritis*, *myalgia*, and *neuralgia*. A plaster may be made by spreading between two layers of thin muslin a paste made by mixing ordinary mustard and wheat flour, equal parts, with warm water. Hot water should not be used, since high temperature destroys the ferment required to evolve the irritant oil from the glucosid. Such a plaster should be left on from 20 to 30 minutes, or until the skin is quite red. A very mild rubefacient effect may be secured by sprinkling a little mustard on the surface of a flaxseed poultice.

Internally, mustard acts as an irritant emetic, evacuating the stomach promptly and thoroughly. It may be employed in cases of *narcotic poisoning*, the dose being a tablespoonful stirred up in warm water, and repeated, if necessary, in 15 minutes.

Thiosinamin (*Allyl-sulphocarbamid*).—This is a compound produced by acting on the volatile oil of mustard with ammonia. It occurs in colorless, soluble crystals, of bitterish taste and a garlicky odor. The reputed action ascribed to it is the softening of scar tissue. Hebra, Unna, Juliusberg, Crocker and Pernet, and others have recommended it in *keloid*, *post-lupus scarring*, *scleroderma*, *elephantiasis*, and *cicatricial strictures and deformities*. It may be given hypodermically every other day, in doses of from 1 to 2 grains (0.06–0.13 gm.), dissolved in glycerin and water, or by the mouth in daily doses of 3 grains (0.2 gm.). Another method of application is by the local use of thiosinamin plasters (10 to 30 per cent.).

Hebra has warned against the use of the drug in all cases of partially healed tuberculous foci.

Fibrolysin.—This is a double salt of thiosinamin and sodium salicylate, freely soluble in water. As the solution is unstable, it is put up in sealed phials, each of which contains 24 grains (1.5 gm.) of fibrolysin, or the equivalent of 3 grains (0.2 gm.) of thiosinamin.

ARNICA, U. S. P.

Arnica is official as the flowers of *Arnica montana*, a perennial herb growing in the temperate regions of Europe, Asia, and America. It contains a volatile oil, tannin, and a glucosid, *arnicin*.

PREPARATION

DOSE

Tinctura Arnicæ, U. S. P. 10-20 min. (0.6-1.3 mls).

Pharmacologic Action and Therapeutics.—Applied to the skin, arnica causes redness and burning, and occasionally very severe erysipelatous inflammation. Internally, according to Hare, moderate doses slow the pulse and raise the blood-pressure. Toxic doses cause gastrointestinal irritation, a feeble pulse, profound prostration, and, sometimes, delirium and stupor.

Arnica, in the form of the tincture, has been used very largely as a stimulant application in *sprains* and *bruises*. Internally, it has been recommended in a variety of diseases, but there is little evidence to show that it is of value in any one of them.

CHRYSAROBINUM, U. S. P.

(Chrysarobin)

Chrysarobin is a neutral principle, more or less impure, obtained from *Goa powder*, a substance found in the wood of *Vouacapoua Araroba*, a large tree growing in the forests of Brazil. It is a yellow, crystalline powder, odorless and tasteless, and very slightly soluble in water, alcohol, chloroform, or ether. On exposure to air it turns brownish, owing to partial oxidation into chrysophanic acid.

PREPARATION

Unguentum Chrysarobini, U. S. P. (6 per cent.).

Pharmacologic Action and Therapeutics.—Chrysarobin is a local irritant and a parasiticide. Internally, large doses cause gastro-enteritis and nephritis. It is eliminated chiefly by the kidneys, partly as chrysophanic acid and partly unchanged.

Although it stains the skin temporarily and the clothing permanently, and, in some persons, causes severe dermatitis, chrysarobin is one of the most efficient remedies we have in *psoriasis*. It is adapted to cases in which the patches are comparatively few and large, or to the large patches in extensive cases (Stelwagon). If used too freely, it may be absorbed and give rise to untoward symptoms. As the conjunctiva is

exceedingly sensitive to its irritant effect, it should not be employed about the face. It may be prescribed in an ointment, 10 to 60 grains (0.65–4.0 gm.) to the ounce (30.0 gm.); suspended in chloroform, 1 to 2 drams (4.0–8.0 gm.) to the ounce (30.0 mils); or suspended in collodion, 30 to 60 grains (2.0–4.0 gm.) to the ounce (30.0 mils). When the infected areas are small, chrysarobin may be applied with advantage also in *ringworm*, either of the body or of the scalp.

OLEUM CADINUM, U. S. P.

(Oil of Cade, Juniper Tar Oil)

Oil of cade is a volatile oil distilled from the wood of *Juniperus Oxycedrus*, a shrub resembling the common juniper and growing in Southern Europe. It is a thick, dark-brown liquid having a tarry odor and taste. It is completely soluble in ether or chloroform and partially so in alcohol.

Therapeutics.—The action of oil of cade is very similar to that of the oil of tar. The drug is chiefly used as a stimulant application in *psoriasis* and *chronic eczema*. It may be prescribed in ointment, 1 to 3 fluidrams (4.0–11.0 mils) to the ounce (30.0 gm.), or as a pigment made by diluting the oil with one or two parts of alcohol.

OLEUM GYNOCARDIÆ

(Oil of Gynocardia, Chaulmoogra Oil)

Chaulmoogra oil is an acrid, whitish fat obtained from the seed of *Taraktogenos kurzii*, a native of the East Indies. Its activity depends upon the glyceryls of certain unsaturated fatty acids, chiefly *chaulmoogric* and *hydnocarpic* acids, which seem to have a destructive action on acid-fast bacilli. The drug has been used, both internally and externally, with asserted good results in *leprosy*. The dose by the mouth is from 5 to 10 minims (0.3–0.6 mil), in capsules, gradually increased, according to tolerance, to $\frac{1}{2}$ to 1 dram (2.0–4.0 mils). Large doses are likely to cause nausea and vomiting. Chaulmoogra oil itself, salts of the fatty acids present in the oil, and ethyl esters of the fatty acids are also given hypodermically. Reports from the subcutaneous injection of the ethyl esters of chaulmoogra acids (antileprol, chaulmestrol) have been especially encouraging, actual cures having occurred in a number of early cases. The injections are given once a week, the dose being gradually increased from 1 mil to 3 or even 5 mils.

BALSAMUM DIPTEROCARPI

(Balsam of Dipterocarpus, Gurjun Balsam, Wood Oil)

Gurjun balsam is an oleoresin obtained by incising *Dipterocarpus turbinatus* and other species of *Dipterocarpus*, large trees growing in India and the East Indies. It contains a volatile oil, gurjunic acid, and resin. It has been used largely to adulterate the oleoresin of copaiba, which it resembles very closely in its properties. It is said to be of value, both as an internal remedy and as a local application in *leprosy*. The dose is from 10 to 40 minims (0.6–2.5 mls), in emulsion. Externally, it is applied by inunction, diluted with from 1 to 3 parts of lime-water or olive oil.

SCARLET RED

(Amido-azo-toluene-azo-beta-naphthol)

Medicinal scarlet red is a dark, reddish brown powder, readily soluble in lard or other fats, but almost insoluble in petrolatum or in water. In the form of 2 to 8 per cent. ointment it has been found useful in stimulating the growth of epithelium on *granulating wounds*, especially *slowly healing burns*, *sluggish leg ulcers*, *bedsores* and *syphilitic sores*. If the ulcer is large the ointment should be applied only around the edges. Severe local irritation and systemic poisoning, characterized by headache, dizziness, faintness, colic and vomiting, have sometimes resulted from the too free use of the 8 per cent. ointment.

OLEUM SUCCINI

(Oil of Amber)

Oil of amber is a volatile oil obtained from the destructive distillation of a fossil resin which is yielded by submerged fir trees washed ashore along the coast of Prussia. It is a thin, transparent, yellow liquid, having a balsamic odor and warm, acrid taste. The dose is 3 to 5 minims (0.2–0.3 ml), in capsules or in an emulsion.

Therapeutics.—Oil of amber was at one time held in high repute as a stimulating liniment for the chest in *whooping cough* and *acute bronchitis*. For infants it should be diluted with 2 or 3 parts of olive oil. Internally, it has been used with asserted good results in *persistent hiccough*.

OTHER COUNTERIRRITANTS

Oil of Turpentine (see p. 255).—In the form of a stupe, oil of turpentine makes an excellent rubefacient application in

a large number of affections attended with pain or irritation, such as *muscular rheumatism*, *intestinal colic*, *gastralgia*, *bronchitis*, and *pulmonary congestion*. Turpentine liniment applied with friction is useful in *myalgia*, *chronic articular rheumatism*, and *chilblain*.

Iodin (see p. 429).—As a counterirritant, iodine is well adapted to conditions requiring a mild but persistent effect. The tincture applied as a pigment is extensively employed in such affections as *laryngitis*, *pleurisy*, *synovitis*, *arthritis*, *neuritis*, *periostitis*, *bubo*, and *chilblain*.

Capsicum (see p. 202).—Tincture of capsicum, more or less diluted, may be applied as a lotion in *acute torticollis* and *chilblain*. Capsicum plaster is sometimes serviceable in relieving *lumbago* and other *muscular pains*.

Chloroform (see p. 124), **Methyl Salicylate** (see p. 419), **Ammonia** (see p. 282), **Camphor** (see p. 141).—These drugs are extensively employed as rubefacients in the form of liniments. They are often combined with advantage, as in the following formula:

R. Methylis salicylatis..... f ʒj (30.0 mils)
Linimenti chloroformi..... q. s. ad f ʒvj (180.0 mils).—M.

ESCHAROTICS OR CAUSTICS

Escharotics or caustics are agents that cause disorganization and death of tissue by direct action. They may act by exciting an inflammatory reaction and bringing about a gradual degeneration of the cells, as in the case of arsenic trioxid; by precipitating protein, as in the case of phenol; by abstracting water and forming acid albuminates, as in the case of the mineral acids; by abstracting water, saponifying the fat and forming alkali albuminates, as in the case of the caustic alkalis; or by precipitating protein, with the formation of metal and acid albuminates, as in the case of metallic salts.

The most important escharotics are:

Sulphuric acid	Chromium trioxid
Nitric acid	Potassium hydroxid
Acetic acid	Sodium hydroxid
Trichloroacetic acid	Sodium ethylate
Lactic acid	Zinc chlorid
Pyrogallic acid	Mercuric nitrate
Osmic acid	Silver nitrate
Phenol	Lead nitrate
Arsenic trioxid	Carbon-dioxid snow

Heat applied by means of the actual cautery (hot iron, Paquelin cautery), the galvanocautery, a monopolar high-frequency current of the Ouidin type (electrodesiccation) or bipolar high-frequency current of the d'Arsonval type (electrocoagulation) is also an effective agent for destroying tissue. Escharotics are used to destroy superfluous granulations, small growths (warts, moles, nevi, superficial epitheliomas, lupus), and the tissue around poisoned wounds, and to modify the specific character of phagedenic ulcers and sloughing wounds.

Depilatories are agents that are used to remove superfluous hair. The most important are *barium sulphid* and *calcium sulphohydrate*. Permanent removal of hair can be effected only by *electrolysis* or *x-ray*.

ACIDUM SULPHURICUM, U. S. P.

(Sulphuric Acid, Oil of Vitriol, H_2SO_4)

Official sulphuric acid is a colorless, heavy, oily liquid, odorless, and of intensely sour taste and acid reaction. It has a marked affinity for water, with which it mixes with the evolution of heat. It rapidly chars and destroys organic matter.

PREPARATIONS

DOSE

Acidum Sulphuricum Dilutum, U. S. P. (contains 10 per cent. of absolute sulphuric acid).	10–20 min. (0.6–1.2 mils)
Acidum Sulphuricum Aromaticum, U. S. P. (an alcoholic solution containing about 20 per cent. of the official acid, with ginger and cinnamon).....	5–20 min. (0.3–1.2 mils).

Pharmacologic Action.—When applied to the skin in concentrated form, sulphuric acid causes intense pain and a rapid destruction of tissue, the eschar being first white and then brown or black. Upon mucous membranes it has a still more irritant and corrosive effect. The local corrosion results from the extraction of water, the neutralization of the alkalis, and the precipitation of proteins. Internally, large doses produce burning in the throat and gullet, violent pain in the abdomen, constant vomiting of dark matter, often mixed with blood and mucus, intense thirst, difficult breathing, and collapse. Death usually occurs within twenty-four hours, and if the acid has reached the larynx, a fatal termination may result almost immediately from suffocation. Blackish stains on the clothing may serve as a clue to the recognition of the poison.

Even in very dilute form sulphuric and other mineral acids, in large doses, may prove fatal to herbivorous animals by overcoming the alkalinity of the blood, thereby rendering it incapable

of removing carbonic acid from the tissues. Such an untoward effect, however, can scarcely occur in carnivorous animals or in man, since in them the tissues under the influence of the acid yield large quantities of ammonia, which unites with acid, thus protecting the alkalis of the blood from neutralization. Sulphuric acid circulates in the blood in the form of its salts, and is rapidly eliminated in the urine chiefly as acid salts.

Treatment of Poisoning.—This consists in administering alkalis—chalk, magnesia, soap, white-wash—together with demulcent drinks, such as albumin-water, milk, or barley-water. Opium is always required to relieve the severe pain. The stomach-pump should, as a rule, be avoided on account of the risk of piercing the softened esophagus.

Therapeutics.—Sulphuric acid, owing to the severity of its action, is less useful as an escharotic than some of the other acids. It is occasionally employed, however, as a caustic in *phagedenic chancroid*, being applied in the form of a paste made by mixing the acid with some indifferent substance, such as charcoal or asbestos.

Internally, in the form of aromatic sulphuric acid, it has been employed as an antihydrotic in the *night-sweats of tuberculosis* but it is without value. Combined with opium, it has been recommended in *serous diarrhea*. Sulphuric acid “lemonade” has been used by workers in lead as a prophylactic against *plumbism* but it is useless.

Administration.—Sulphuric acid should be given well diluted, precautions being taken to prevent its action on the teeth.

Incompatibles.—Alkalis, alkaline carbonates, iodids, and salts of lead and of calcium. It is explosive with sugar and oil of turpentine. The undiluted acid carbonizes syrups.

ACIDUM NITRICUM, U. S. P.

(Nitric Acid, HNO_3)

The official nitric acid is a colorless, intensely acid, fuming liquid composed of 68 per cent. of absolute nitric acid and 32 per cent. of water.

PREPARATIONS

DOSE

Acidum Nitricum Dilutum (10 per cent. by weight of absolute nitric acid).....	5-20 min. (0.3-1.2 mils)
Acidum Nitrohydrochloricum, U. S. P. (aqua regia: Nitric acid, 18; hydrochloric acid, 82)...	2-4 min. (0.1-0.25 mils)
Acidum Nitrohydrochloricum Dilutum, U. S. P. (nitric acid, 4; hydrochloric acid, 18; water, 78).....	5-20 min. (0.3-1.2 mils).

Pharmacologic Action and Therapeutics.—Locally, pure nitric acid is a powerful caustic, but somewhat less painful and less penetrant than sulphuric acid. It stains the skin yellow. In overdoses it produces symptoms and lesions (except the yellow coloration) similar to those produced by sulphuric acid, and in poisoning the same treatment is applicable.

As an escharotic, nitric acid is generally preferred to other mineral acids, as its action is more readily controlled. It has been found reliable in *phagedenic ulcers*, *chancroids*, and *chancres*, and in *hospital gangrene*. It has been used successfully also, when milder measures have failed, as a means of producing inflammatory contractile tissue in *prolapse of the rectum* occurring in children.

Internally, dilute nitric acid has been recommended by Ringer and others in *indigestion*, especially when eructation of offensive gas is a prominent symptom, or when there is a tendency to persistent aphthous stomatitis. It should be taken well diluted through a glass tube.

Incompatibles.—Alkalis, carbonates, oxids, lead acetate, and iron sulphate. The strong acid forms explosive compounds with readily oxidizable substances, such as glycerin, alcohol, phenol, resins, volatile oils, etc.

Nitrohydrochloric Acid.—This is a yellow, fuming, corrosive liquid produced by mixing nitric acid with hydrochloric acid. Both acids undergo decomposition with the formation of nitrosyl chlorid (NOCl) and chlorin. Nitrohydrochloric acid is believed to have a special action on the liver, and has been used with asserted good results in so-called *biliousness*, *catarrhal jaundice*, *cirrhosis of the liver*, etc., but its efficiency is doubtful. It should be taken after meals, well diluted, through a tube. It should not be prescribed undiluted with tinctures or other alcoholic preparations, as such mixtures are liable to explode.

Nitrohydrochloric acid is not used as an escharotic.

ACIDUM ACETICUM

(Acetic Acid, $\text{HC}_2\text{H}_3\text{O}_2$)

Acetic acid is official in the following forms:

Acidum Aceticum, U. S. P. (36 per cent. by weight of absolute acetic acid)

Acidum Aceticum Dilutum, U. S. P. (6 per cent. by weight of absolute acetic acid)

Acidum Aceticum Glaciale, U. S. P. (nearly absolute acetic acid).

Vinegar (*acetum*) is not official, but has the same therapeutic lue as diluted acetic acid.

Pharmacologic Action and Therapeutics.—Locally applied, concentrated acetic acid produces redness, vesication, and ultimately superficial sloughing. Taken internally, it causes severe gastritis. Even small doses of acetic acid, if long continued, may cause chronic gastric catarrh. It is eliminated as carbonates, so it does not increase the acidity of the urine.

Glacial acetic acid is sometimes employed to remove *warts* and *corns*. Inhalations of diluted acetic acid or of vinegar are often useful in checking vomiting occurring after general anesthesia. Vinegar is of service as a local hemostatic in *epistaxis*, *leech-bites*, and *small wounds*. In the form of an enema, it is occasionally employed to destroy *oxyures*. Internally, it may be used as an antidote in *poisoning by alkalis*.

ACIDUM TRICHLORACETICUM, U. S. P.

(Trichloroacetic Acid, $\text{HC}_2\text{Cl}_3\text{O}_2$)

Trichloroacetic acid is formed by acting on glacial acetic acid with chlorine or on hydrated chloral with fuming nitric acid. It occurs in colorless, hygroscopic crystals, of pungent odor and strongly acid reaction.

Therapeutics.—Pure or in concentrated solution, trichloroacetic acid has been used successfully as a caustic for removing small cutaneous growths, such as *venereal* or *common warts*, *pigmented moles*, *nevi*, and *corns*. It may be applied with a toothpick wrapped with cotton, the skin having first been cleansed with benzine to facilitate the penetration of the acid. A solution of from 5 to 10 per cent. also makes an excellent stimulant application in *chancroids*, *mucous patches*, *tuberculous ulcers*, and *fistulous tracts*. In this strength it causes but little pain or inflammatory reaction.

ACIDUM LACTICUM, U. S. P.

(Lactic Acid, $\text{CH}_3\text{CHOH.COOH}$)

Lactic acid is an organic acid usually obtained by subjecting milk-sugar or grape-sugar to lactic fermentation. The official preparation contains from 85 to 90 per cent. of absolute lactic acid.

Therapeutics.—Lactic acid in solutions of from 20 to 100 per cent. makes a useful application in *tuberculous* and *lupous ulcerations of mucous membranes*. In the proportion of 1 part of the acid to from 5 to 20 parts of water it sometimes proves efficacious in *freckles* and *chloasma*.

PYROGALLOL, U. S. P.

(Pyrogallie Acid, $C_6H_3(OH)_3$)

Pyrogallie acid is produced by the action of heat on gallic acid. It occurs in white, lustrous needles or scales, odorless, and of a bitter taste. It is readily soluble in water, alcohol, or ether.

Pharmacologic Action and Therapeutics.—Locally, pyrogallol is an irritant or caustic, according as it is applied in dilute or in concentrated form. It is also an active parasiticide. It stains the skin a brownish color. As a caustic its action is slow and attended with but little pain. Owing to its power to destroy the red blood-cells and to convert hemoglobin into methemoglobin, grave, or even fatal, toxic effects may result from the application of the drug over too large a surface.

Pyrogallol is an efficient caustic in *lupus* and *epithelioma*, when the lesions are small. It is generally applied in the form of an ointment, from 20 to 40 per cent. in strength. Stelwagon recommends the following formula:

℞. Pyrogallol..... ʒij-ijj (8.0-12.0 gm.)
 Cerati resinæ
 Petrolati..... āā q. s. ad ʒj (30.0 gm.).—M.

Such an ointment should be applied on lint, and renewed twice a day for two or three weeks, the superficial sloughs being removed every few days by poulticing or gentle scraping.

An ointment containing from 20 to 60 grains (1.3-4.0 gm.) of pyrogallol to the ounce (30.0 gm.) is sometimes useful in *psoriasis*.

ACIDUM OSMICUM

(Osmic Acid, Osmium Tetroxid, OsO_4)

Osmic acid occurs in yellow, crystalline needles, having a pungent odor and a burning taste. It is readily soluble in water, alcohol, or ether.

Therapeutics.—Even in weak solution, it is exceedingly irritant and caustic. Stekoulis, Schapiro, Bennett, and others claim excellent results from injections of osmic acid in *neuralgia*. The nerve having been exposed by a small incision, a 1.5 per cent. solution, freshly prepared, is injected into it at several points, to the amount of from 5 to 10 minims (0.3-0.6 mil). The blood and tissues are stained intensely black by the acid, but healing of the wound is said to proceed rapidly without suppuration.

CHROMII TRIOXIDUM, U. S. P.

(Chromium Trioxid, Chromic Acid, Chromic Anhydrid, CrO_3)

Chromium trioxid, or so-called chromic acid, occurs in crimson, deliquescent crystals, odorless, and readily soluble in water. With organic matter, alcohol, glycerin, ether, tannin, sugar, etc., it is explosive.

Pharmacologic Action and Therapeutics.—Owing to its strong oxidizing power, chromic acid is an energetic caustic, slower and somewhat less painful in its action, however, than nitric acid, potassa, or silver nitrate. Internally, it is an active poison, producing severe abdominal pain, vomiting, purging, albuminuria, and collapse. The vomited matters are often of a green or bluish-green color. The postmortem lesions consist in inflammation and erosion of the gastrointestinal mucous membrane, nephritis, and fatty degeneration of the tissues, especially of the liver. Alkalis neutralize the acid, but as they form poisonous salts, the stomach should be thoroughly emptied after their administration. The local application or inhalation of chromium compounds may also result in poisoning. Workers in these preparations not infrequently suffer from ulcerations of the skin and mucous membranes, chronic bronchitis, and diffuse nephritis.

Chromic acid may be used to destroy small growths, such as *common warts*, *venereal warts*, and *corns*. For this purpose it may be applied in substance or in strong solution—2 to 3 drams (8.0–12.0 gm.) to the ounce (30.0 mls). The fused acid on a probe may also be employed successfully in removing *soft hypertrophies* of the nasopharyngeal mucous membrane and in closing small *salivary fistulæ*. A solution of from 20 to 30 grains (1.3–2.0 gm.) to the ounce (30.0 mls) makes an excellent stimulant application in *mucous patches*. A solution of 40 grains (2.6 gm.) to the ounce (30.0 mls), applied once a week, has been well recommended in *hyperidrosis* and *bromidrosis of the feet*.

POTASSII HYDROXIDUM, U. S. P.

(Potassium Hydroxid, Caustic Potash, KOH)

Caustic potash occurs in hard white pencils or fused masses, odorless, deliquescent, strongly alkaline, and corrosive. It is soluble in 0.9 part of water or in 3 parts of alcohol.

PREPARATION

DOSE

Liquor Potassii Hydroxidi, U. S. P. (5 per cent.) 5–20 min. (0.3–1.2 mls).

Pharmacologic Action and Therapeutics.—In concentrated form, potassium hydroxid is a diffusive and deeply pene-

trating escharotic. Its action is rapid and painful. It produces a grayish, soft, and pultaceous slough, which separates in a few days, leaving an ulcer. Its caustic properties are due to the power of its hydroxyl molecule to abstract water from the tissues, to soften and dissolve them, and to form with the proteins a soluble alkaline albuminate. When swallowed in strong solution it produces all the symptoms of a violent corrosive poison—burning in the throat and gullet, intense abdominal pain, vomiting and purging of mucous and bloody matter, dysphagia, hoarseness, and collapse. If recovery follows, stricture of the esophagus or cicatricial contractions of the stomach are likely to result from the extensive ulceration.

Small doses, in dilute solution, exert an influence similar to that of the alkaline carbonates (see Gastric Antacids). The drug is eliminated as a carbonate, chiefly in the urine.

Treatment of Poisoning.—This consists in neutralizing the alkali with a weak acid, such as vinegar or lemon-juice, and in allaying the irritation and pain with demulcents and opium.

As an escharotic, caustic potash may be used to remove *common warts* and small *cutaneous cancers*. For this purpose the solid stick should be used, the surrounding parts being protected by a coating of oil. When the desired effect has been attained, further action may be prevented by the application of vinegar. Caustic potash is also an efficient agent with which to cauterize the *bites of rabid animals*. In *ingrowing toe-nail*, the insertion under the nail of a pledget of cotton soaked in liquor potassii hydroxidi (1 part to 4 parts of water) affords an excellent means of removing the redundant tissue, thus facilitating the raising of the nail. The diffusive action of potassium hydroxid renders it unsuitable for use on mucous membranes.

A mixture of equal parts of potassium hydroxid and lime (*Vienna paste*), being less deliquescent than pure caustic potash, is more manageable than the latter, but slower in its action.

Internally, solution of potassium hydroxid, well diluted, is rarely used as an *antacid*.

Incompatibles.—Acids, acid salts, metallic salts, and alkaloids.

SODII HYDROXIDUM, U. S. P.

(Sodium Hydroxid, Caustic Soda, NaOH)

Caustic soda occurs in white, translucent pencils or fused masses, odorless, of an acrid, caustic taste and an intensely alkaline reaction. It is readily soluble in water or in alcohol.

PREPARATION

DOSE

Liquor Sodii Hydroxidi, U. S. P. 5-20 min. (0.3-1.2 mls).

Therapeutics.—Caustic soda may be used for the same purposes as caustic potash, the action of the two drugs being similar.

SODII ETHYLAS

(Sodium Ethylate, Sodium Alcohol, $\text{NaC}_2\text{H}_5\text{O}$)

A solution of sodium ethylate, made by dissolving 1 part of metallic sodium in 20 parts of absolute alcohol, has been used, on the recommendation of B. W. Richardson, as a caustic to remove *vascular nevi* and *warts*. It should be applied with a glass rod, and the superficial dry crust formed allowed to come off spontaneously. It is said to cause less scarring than other caustics. It is decomposed by water.

BROMUM, U. S. P.

(Bromin, Br)

Bromin is a non-metallic element obtained from sea-water. It is a dark, reddish-brown liquid, evolving, even at ordinary temperatures, suffocating and irritating fumes. It is soluble in 28 parts of water and readily soluble in alcohol or ether.

Pharmacologic Action and Therapeutics.—Bromin is an intensely active and painful escharotic. It is also a disinfectant and deodorant. When ingested, it causes inflammation and extensive necrosis of the gastrointestinal mucosa. Inhaled, it acts like chlorin, producing mucopurulent bronchitis, edema of the lungs, and foci of catarrhal pneumonia.

Bromin has been used as an escharotic in *phagedenic* and *cancerous ulcerations*, but, owing to the difficulty in handling it and the great pain caused by its application, it is rarely employed at the present time. It is still occasionally used in very weak solutions as a *deodorant* (see p. 443).

Bromipin.—This preparation is an addition-product of sesame oil and bromin (10 per cent.). It is a yellowish, oily liquid, free from the caustic properties of bromin. In daily doses of from 1 to 3 fluidrams (4.0-11.0 mls) it has been used with asserted good results as a substitute for the bromids in *epilepsy*.

SOLID CARBON DIOXID

(Carbon-dioxid Snow)

Carbon-dioxid snow provides a rapid and efficient means of removing by freezing certain small lesions of the skin, such as

warts, nevi, patches of lupus erythematosus, superficial epitheliomas, etc. It has an advantage over liquid air in being easily procurable, although the latter acts more rapidly, its temperature being 190° C., while that of solid carbon dioxid is only 78.2° C. Stelwagon directs that the snow be obtained by tying a somewhat thick chamois skin in the form of a pocket over the nozzle of one of the small cylinders of liquid carbon dioxid sold by automobile-supply houses. When the cylinder is held perpendicularly down and the gas turned on the snow collects in the chamois pocket. A pencil may be formed of the snow by packing it firmly into a hard-rubber mold, such as an ear speculum. In making the application the pencil is held with a small piece of chamois and pressed somewhat firmly upon the diseased patch for from 15 to 60 seconds. The frozen area thaws out in a few minutes, becomes red, and later is transformed into a thin crust, which eventually drops off leaving a scarcely noticeable scar. Burning and tingling accompany the thawing, but, as a rule, there is not much pain.

BARIUM SULPHIDUM

(Barium Sulphid, BaS)

Barium sulphid is an amorphous, pale yellow, phosphorescent powder, soluble in water. Diluted with from 1 to 3 parts of some inert powder, it is used as a *depilatory*. Duhring recommends:

R̄. Barii sulphidi..... ʒj-ij (4.0-8.0 gm.)
Amyli
Zinci oxidi..... āā ʒiss (6.0 gm.).—M.

At the time of application sufficient water is added to make a paste, which is thickly spread over the affected part and allowed to remain for a minute or two or until it excites slight burning.

Barium sulphid deteriorates with age and on exposure to air.

CALCII SULPHIDUM HYDRATUM

(Hydrated Calcium Sulphid, Calcium Sulphohydrate, $\text{CaS} + \text{H}_2\text{O}$)

Hydrated calcium sulphid is a whitish or pale-pink powder, made by heating together at a high temperature calcium sulphate and granulated wood-charcoal. In the form of a paste, it has been recommended by Kaposi, Brayton, and others as a harmless *depilatory*. When wetted, it gives off hydrogen sulphid, which is sometimes a drawback to its use.

OTHER ESCHAROTICS

Arsenic Trioxid (see p. 313).—Arsenic is a slowly acting but deeply penetrating escharotic. It causes severe pain and considerable inflammatory swelling, and, if applied over too large a surface, may prove dangerous through absorption. On the other hand, its action, while very thorough, is largely limited to the diseased tissue. Its *modus operandi* is not definitely known, but as it does not combine chemically with the tissues, it is supposed to act indirectly by exciting a violent inflammatory reaction and directly upon the cells in a specifically poisonous manner. The employment of arsenic as an escharotic is practically confined to the removal of *small cutaneous cancers* and *lupus infiltrations* (see p. 318) and the destruction of the *pulp in carious teeth*.

Phenol (see p. 405).—Phenol is a comparatively superficial escharotic, the deeper tissues being protected by an albuminous coagulum. Owing to the property which it possesses of paralyzing the peripheral sensory nerves, its application is not followed by very severe or persistent pain. Absolute alcohol destroys its caustic action. After thorough curettement of the parts pure liquid phenol may be applied with advantage in *inflammatory gangrene*, *irritable ulcers*, *carbuncles*, and *fistulæ*.

Mercuric Nitrate (see p. 399).—This salt is an exceedingly irritant and powerful escharotic. Its action depends upon several factors: (1) The union of the metal with the proteins to form a soluble albuminate; (2) the liberation of nitric acid, which is also caustic; and (3) the toxic effects upon the cells of the mercury itself. As an escharotic it has been extensively employed in the form of the solution of mercuric nitrate in *phagedenic venereal sores*. If used too freely, it is liable to be absorbed and to induce salivation.

Zinc Chlorid (see p. 367).—This salt is an energetic and very painful caustic. It produces a dry, whitish slough, the separation of which usually requires from one to three weeks. Unlike arsenic, it does not spare the healthy tissue. In the form of a paste to which cocain has been added, it is sometimes used to remove *cutaneous epitheliomata*.

Silver Nitrate (see p. 369).—The insoluble and impenetrable pellicle of silver albuminate which lunar caustic immediately forms when brought in contact with the tissues confines its destructive action to the superficial cells. In the form of the solid stick it is an excellent caustic for removing such formations as *small warts*, *mucous patches*, and *superfluous granulations*.

Lead Nitrate (see p. 358).—The corrosive action of this salt of lead is due largely to the nitric acid which is liberated when it is brought in contact with proteins. It has been used to some extent in the form of a powder as a caustic in *onychia*.

PROTECTIVES

Protectives are agents that serve to protect inflamed or injured surfaces from external irritation. Their action is chiefly mechanical. Those of a mucoid or colloid nature, which exert a soothing effect upon inflamed parts, are known as **demulcents**. The most important members of this subdivision are:

Flaxseed	Marshmallow
Acacia	Licorice root
Tragacanth	Almond
Slippery elm	Starch
White and yolk of egg.	

Internally, demulcents are especially useful in protecting the walls of the stomach from the action of corrosive poisons. Made up into lozenges and allowed to dissolve slowly in the mouth, they tend to subdue pain and cough resulting from irritation of the throat. In the form of enemata, they are used to relieve the tenesmus of acute dysentery. Externally, they are rarely employed except in the form of poultices, and even in this form they are used more as a means of applying heat and moisture than as protectives. Hot poultices are sometimes efficacious in relaxing local spasms, such as occur in asthma and the various forms of colic. In deep-seated inflammations—pyelitis, nephritis, cystitis, etc.—they usually afford considerable comfort, and no doubt exert a reflex influence on the morbid process itself (see Counterirritants). In superficial inflammations hot antiseptic fomentations have largely supplanted ordinary poultices, because the latter afford such excellent media for the growth of bacteria. When suppuration has already occurred or is obviously inevitable, poultices are wholly inadmissible.

Protectives of a fatty character, intended to shield the skin from external irritants and at the same time to soften and relax it, are known as **emollients**. The most important are:

Lard	Almond oil
Suet	Linseed oil
Wool-fat	Petrolatum
Spermaceti	Glycerin
Olive oil	Wax
Cotton seed oil.	

Emollients are used for their protective and soothing properties in burns, in fissuring of the lips and hands, and in acute inflammatory diseases of the skin. They are also extensively employed as bases for special ointments.

The so-called **dusting-powders** constitute another group of protectives. The requisites of a good dusting-powder are dryness, insolubility, inertness, and absolute freedom from grittiness. Those in common use are:

Starch	Zinc oxid
Talc	Chalk
Kaolin	Magnesium carbonate
Lycopodium.	

Dusting-powders are prescribed in various forms of erythema and in acute eczema to protect the parts from air, moisture, and friction.

Finally, certain protectives which have strong adhesive properties and can be kept in place for several days without change are employed as **fixed dressings**. In this class are:

Collodion	Solution of gutta-percha.
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Lead plaster (*Emplastrum Plumbi*, U. S. P.) and adhesive or rubber (*Emplastrum Elasticum*, U. S. P.), also belong in this group.

Fixed dressings are frequently of service in the treatment of abrasions, small wounds, fissures, and bed-sores.

LINUM, U. S. P.

(Linseed, Flaxseed)

Linseed is the seed of *Linum usitatissimum*, or common flax, an annual cultivated in all temperate countries. From a therapeutic viewpoint its chief ingredients are a mucilaginous principle and a fixed oil.

PREPARATIONS

Oleum Lini, U. S. P.

Linimentum Calcis, U. S. P. (Carron-oil: equal parts of linseed oil and lime-water)

Liquor Cresolis Compositus, U. S. P.

Therapeutics.—An infusion or tea of flaxseed serves as an excellent *demulcent drink*. Ground flaxseed is the material most commonly selected for making ordinary *poultices*. Soft soap and liniment of soft soap are used for detergent purposes and also for removing *crusts* and *scales* in sluggish diseases of the skin, such as seborrhea and psoriasis.

ACACIA, U. S. P.

(Gum Arabic)

Acacia is a gummy exudation obtained from *Acacia Senegal*, a small tree growing in Senegal, Kordofan, and Abyssinia. It contains *arabic acid* in combination with calcium, magnesium, and potassium.

PREPARATIONS	DOSE
Mucilago Acaciæ, U. S. P.....	Indefinite
Syrupus Acaciæ, U. S. P.....	Indefinite
Pulvis Cretæ Compositus, U. S. P.....	5-60 gr.(0.3-4.0 gm.)

Acacia also enters into chalk mixture, compound mixture of glycyrrhiza, emulsion of almond, emulsion of cod-liver oil, emulsion of oil of turpentine, troches of cubeb, and several pills.

Therapeutics.—In therapeutics acacia is used chiefly as a *demulcent*, although a 5 or 6 per cent. sterile solution in normal salt solution has been used for transfusion in cases of *shock*, *severe hemorrhage*, etc. The drug does not cause hemolysis, but chills sometimes follow the injection and occasionally there is serious collapse. In pharmacy it is used for holding together the active ingredients in pills and lozenges and for suspending insoluble substances in water. It is precipitated from its solution by alcohol, subacetate of lead, ferric salts, and borax.

TRAGACANTHA, U. S. P.

(Tragacanth)

Tragacanth is a gummy exudation from *Astragalus gummifer*, a shrub growing in western Asia. It contains *traganthin* or *bassorin* and the *calcium salt of gummic acid*. It swells up in water into a gelatinous mass, but, unlike acacia, does not dissolve in it.

PREPARATION

Mucilago Tragacanthæ, U. S. P.

Tragacanth also enters into most of the official troches.

Therapeutics.—On account of its insolubility, it is rarely used as a demulcent. It is employed in pharmacy for suspending resins, oils, and heavy powders in water. An excellent lubricating jelly may be prepared according to the following formula:

R. Tragacanthæ.....	gr. xlv (3.0 gm.)
Glycerini.....	f 3viss (25.0 mls)
Phenolis.....	gr. xx (1.3 gm.)
Aquæ destillatæ.....	q. s. ad f 3x (300.0 mls).—M.

Break the tragacanth into fragments, put them in a wide-mouthed bottle, add the other ingredients, and shake the bottle at short intervals.

ULMUS, U. S. P.

(Slippery Elm)

Slippery elm is the inner bark of *Ulmus fulva*, a large tree growing in the Eastern States of North America. It contains a large quantity of mucilaginous matter.

Therapeutics.—The powdered bark is sometimes used instead of flaxseed meal for making small *poultices*. In the form of lozenges it is sometimes employed for its soothing properties in *pharyngitis*.

ALTHÆA, U. S. P.

(Marshmallow Root)

Marshmallow is the root of *Althæa officinalis*, a perennial herb growing in most temperate countries. It contains a large amount of mucilage and of starch. It is an ingredient of blue-mass, pills of phosphorus, and pills of carbonate of iron.

Therapeutics.—Although it is an agreeable demulcent, marshmallow is rarely prescribed at the present time.

GLYCYRRHIZA, U. S. P.

(Licorice Root)

Glycyrrhiza is the root of *Glycyrrhiza glabra typica*, or *Glycyrrhiza glabra glandulifera*, a perennial herb growing in southern Europe and western Asia and cultivated in England and the United States. It contains a glucosid, *glycyrrhizin*, to which it owes its sweet taste.

PREPARATIONS	DOSE
Extractum Glycyrrhizæ, U. S. P.	Indefinite
Extractum Glycyrrhizæ Purum, U. S. P.	Indefinite
Glycyrrhizinum Ammoniatum, U. S. P.	3-10 gr. (0.2-0.65 gm.)
Fluidextractum Glycyrrhizæ, U. S. P.	½-1 fl. dr. (2.0-4.0 mils)
Mistura Glycyrrhizæ Composita, U. S. P. (brown mixture: Pure extract of licorice, 3; syrup, 5; acacia, 3; paregoric, 12; tartar emetic, 0.02; spirit of nitrous ether, 3; water to make 100).	1-4 fl. dr. (4.0-15.0 mils)
Pulvis Glycyrrhizæ Compositus, U. S. P. (gly- cyrrhiza, 23.6; senna, 18; washed sulphur, 8; fennel oil, 0.4; sugar, 50).	½-2 dr. (2.0-8.0 gm.)
Elixir Glycyrrhizæ, U. S. P. (fluidext. glycyrrhizæ, 12.5; aromatic elixir, 87.5).	

Glycyrrhiza also enters into aromatic fluidextract of cascara sagrada, compound fluidextract of sarsaparilla, compound syrup of sarsaparilla, tincture of aloes, mass of mercury, pills of

ferrous iodid, troches of ammonium chlorid, and troches of cubeb.

Glycyrrhizin, which is made soluble with the aid of ammonia, is precipitated from the fluidextract by acids.

Therapeutics.—Licorice is a popular remedy for *cough* resulting from irritation of upper respiratory tract. It is also largely employed to cover the disagreeable taste of other medicines.

AMYGDALA

(Almond)

Almonds are official in two forms: Bitter almonds (*Amygdala Amara*, U. S. P.) and sweet almonds (*Amygdala Dulcis*, U. S. P.). Both varieties contain a *fixed oil* and a ferment, *emulsin*. Bitter almonds contain also a glucosid, *amygdalin*, which, in the presence of water, is acted upon by the emulsin and broken up into hydrocyanic acid, benzaldehyd, and glucose. Oil of bitter almond (*Oleum Amygdalæ Amaræ*, U. S. P.) is a loose combination of hydrocyanic acid (2.0–4.0 per cent.) and benzaldehyd (85 per cent.), obtained by distillation. As sweet almonds do not contain amygdalin, they do not yield hydrocyanic acid when triturated with water.

PREPARATIONS

DOSE

Oleum Amygdalæ Amaræ, U. S. P.	¼–1 min. (0.016–0.06 mil)
Benzaldehydum, U. S. P. (an aldehyd produced artificially or obtained from oil of bitter almond, and having the odor and taste of the latter)	¼–1 min. (0.016–0.06 mil)
Oleum Amygdalæ Expressum, U. S. P.	
Aqua Amygdalæ Amaræ, U. S. P. (¼ per cent. of oil of bitter almond)	½–2 fl. dr. (2.0–8.0 mils)
Spiritus Amygdalæ Amaræ, U. S. P. (1 per cent. of oil of bitter almond)	5–20 min. (0.3–1.2 mils)
Emulum Amygdalæ, U. S. P. (6 per cent. of sweet almond)	2–4 fl. dr. (8.0–15.0 mils).
Unguentum Aquæ Rosæ, U. S. P. (cold cream: spermaceti, 12.5; white wax, 12; expressed oil of almond, 56; stronger rose-water, 19; sodium borate, 0.5).	

The expressed oil of almond also enters into the emulsion of oil of turpentine.

Therapeutics.—Almond is nutritive and demulcent. As almond flour contains no starch, it may be used, after the sugar and gum have been extracted from it, as a *diabetic food*. Expressed oil of almond, ointment of rose-water, and emulsion of

almond are useful *emollients*. Syrup of almond is employed chiefly as a pleasant vehicle. Oil of bitter almond is an active poison. It was for a time used as a substitute for hydrocyanic acid, but its uncertain composition proved to be a disadvantage. It is now rarely employed except as a flavoring agent.

AMYLUM, U. S. P.

(Corn Starch)

Official starch is the fecula of the seed of *Zea mays*, or Indian corn. Wheat-starch and rice-starch are also used in therapeutics.

PREPARATION

Glyceritum Amyli

Therapeutics.—Finely powdered starch is much used as an absorbent and protective application in *erythema intertrigo*, or *chafing*. As it readily decomposes in the presence of heat and moisture, boric acid should be added to it as a preservative. The starch poultice, made by mixing starch with cold water and then adding boiling water until the mass is converted into a gelatinous paste, is sometimes employed to remove *crusts* in chronic inflammatory diseases of the skin. Starch-and-laudanum enemata, made by adding laudanum to thin starch mucilage, are often efficacious in *acute dysentery* and other *inflammatory diseases of the rectum*. Starch is an antidote to *iodin-poisoning*.

ADEPS LANÆ, U. S. P., AND ADEPS LANÆ HYDROSUS, U. S. P.

(Wool-fat and Hydrous Wool-fat, Lanolin)

Wool-fat is the purified fat of the wool of sheep, freed from water, and hydrous wool-fat is wool-fat mixed with not more than 30 per cent. of water. Both preparations are yellowish-white, unctuous substances, having a faint peculiar odor.

Hydrous wool-fat enters into belladonna ointment, stramonium ointment, ointment of ammoniated mercury, and ointment of yellow mercuric oxid.

Therapeutics.—Hydrous wool-fat was introduced by Liebreich, under the name of lanolin, as a vehicle for external medicaments. As an ointment base it is bland and unirritating, does not become rancid, and is miscible with twice its weight of water without losing its ointment-like character; but the claim that it has greater penetrating power than all other fats is not borne out by experience. Singly, it is an unsatisfactory base,

but it sometimes makes a valuable addition to other bases, especially when aqueous substances are to be incorporated.

In certain skin diseases ointments containing water are objectionable; in such cases the anhydrous preparation of wool-fat should be chosen.

CETACEUM, U. S. P.

(Spermaceti)

Spermaceti is a concrete fatty substance obtained from the head of the sperm-whale (*Physeter macrocephalus*). It occurs in pearly-white, translucent masses, odorless, and of a bland, mild taste. It is employed chiefly to give proper consistence to cerates and ointments.

PREPARATION

Unguentum Aquæ Rosæ, U. S. P. (12.5 per cent.)

OLEUM OLIVÆ, U. S. P.

(Olive Oil, Sweet Oil)

Olive oil is a fixed oil expressed from the ripe fruit of *Olea europæa*.

Therapeutics.—Externally, olive oil is a useful emollient. With carbolic acid (5 per cent.) it makes a soothing, protective application for *superficial burns*. In *scarlatina* and *measles* daily inunctions of olive oil are of service in allaying irritation of the skin and in preventing diffusion of the scales. It may be employed to soften *adherent crusts* in such diseases as eczema and seborrhea. Enemata of olive oil (6–8 oz.—175.0–235.0 mls) are very efficacious in removing *fecal concretions* from the rectum. Internally, its effects are nutritive, demulcent, and feebly laxative. Leube and others have employed, with good results, daily subcutaneous injections of olive oil (2–6 oz.—60.0–175.0 mls) as a means of nourishing patients with stricture of the esophagus, but the treatment is not without danger. In one instance, at least, it was the cause of fatal oil-embolism. By some authorities olive oil is held in high repute as a remedy for *gall-stones*, but its value is somewhat doubtful. Five or six ounces (150.0–175.0 mls) are given in the attacks of colic, and smaller doses in the intervals. If the drug possesses any efficacy in cholelithiasis, this may depend upon an antispasmodic influence exerted upon the common bile-duct, as Cohnheim has found large doses of the oil very beneficial in *gastrectasis* depending upon *spasm of the pylorus* from ulcer or fissure, and Weill, Duplant, and others have spoken highly of olive oil in *lead-colic*.

OLEUM GOSSYPII SEMINIS, U. S. P.

(Cottonseed Oil)

Cottonseed oil is a fixed oil expressed from seeds of cultivated varieties of *Gossypium herbaceum*, a shrub cultivated in the southern United States and in many other warm countries. It is employed in the preparation of soft soap (*Sapo Mollis*, U. S. P.), liniment of soft soap (*Linimentum Saponis Mollis*, U. S. P.) and camphor liniment (*Linimentum Camphoræ*, U. S. P.). It has properties similar to those of olive oil, for which it may often be substituted advantageously, owing to its inexpensiveness.

PETROLATUM

(Paraffin, Cosmolin, Vaseline)

Petrolatum is a mixture of hydrocarbons, chiefly of the marsh-gas series, obtained by distilling off the more volatile portions of petroleum and purifying the residue when it has the desired melting-point. Three forms are official: petrolatum (*Petrolatum*), a yellowish mass, of the consistence of an ointment; white petrolatum (*Petrolatum Album*), a white mass, of the consistence of ointment; and liquid petrolatum (*Petrolatum Liquidum*), a colorless, transparent, oily liquid.

Therapeutics.—Petrolatum is largely used as an emollient and protective dressing and as a substitute for animal and vegetable fats in ointments. It is bland and unirritating, and has little tendency to change. It probably has somewhat less penetrating power than lard.

Subcutaneous and submucous injections of paraffin have been employed with more or less success for the correction of various defects and for cosmetic purposes. Thus, they have been used in preventing rectal and vaginal prolapse, in relieving incontinence of urine and feces, and in correcting nasal deformities, etc. The paraffin, with a melting-point of from 38° to 40° C., is sterilized, and then injected while warm and semisolid. As a rule, the effect is not permanent, the paraffin being gradually replaced by cicatricial tissue. Occasionally, too, the local irritation has resulted in tumor-formation. Preparations of paraffin, solid at the body-temperature, but more ductile and pliable than the official preparation (melting at 47° to 50° C., pliable at or below 28° C., and ductile at or below 30° to 31° C.) make an excellent dressing for *burns*, especially burns of the first and second degree. Various brands are on the market and are known as surgical paraffin, surgical wax, parresine, ambrine, etc. The burn is washed with sterile water and dried by fanning. Blisters are not opened. A thin coating of liquid paraffin is

then applied by means of an atomizer or camel's-hair brush. Over this is placed a thin film of cotton wool, which in turn is heavily sprayed with the melted paraffin (about 53° C.). A wool bandage completes the dressing. The dressing should be changed at first daily and later every other day. At the second dressing blisters are opened and the dead skin cut away. A similar paraffin dressing is also useful in *herpes zoster*.

Internally, colorless, water-white liquid petrolatum, free from odor and taste, is often of service in the treatment of *spastic constipation* (see p. 215). The more viscid oils of a specific gravity of about 0.885 to 0.890 are usually preferred, as the lighter oils are thought to pass more rapidly through the bowel and to be more likely to dribble or leak from the anus. The light oils are preferable in the making of solutions and sprays to be used as local applications.

GLYCERINUM, U. S. P.

(Glycerin, $C_3H_5(OH)_3$)

Glycerin is a liquid obtained from fats and fixed oils by saponification with alkalis or by the action of superheated steam. It is a clear, colorless, hygroscopic liquid, of syrupy consistence, having a slight, characteristic odor and a sweet taste, and producing a sensation of warmth in the mouth. It is miscible with water or alcohol, but is insoluble in chloroform, ether, or oils. The dose is from 1 to 4 fluidrams (4.0–15.0 mls).

PREPARATIONS

Glyceritum Phenolis, U. S. P. (20 per cent. of phenol)

Glyceritum Acidi Tannici, U. S. P. (20 per cent. of tannic acid)

Glyceritum Amyli, U. S. P. (plasma: starch, 10; water, 10; glycerin, 80)

Glyceritum Boroglycerini, U. S. P. (50 per cent. of boroglycerin)

Glyceritum Hydrastis, U. S. P. (each mil contains 1.12–1.37 grams of ether-soluble alkaloids)

Suppositoria Glycerini, U. S. P. (each suppository contains 45 gr.—3.0 gm. —of glycerin, solidified by sodium stearate)

Gelatinum Glycerinatum, U. S. P. (gelatin and glycerin, of each, 100 gm.; water to make, 200 gm.)

Cataplasma Kaolini, (kaolin, 57.7 parts; boric acid, 4.5 parts; glycerin, 37.5 parts; with small quantities of methyl salicylate, thymol, and oil of peppermint).

Pharmacologic Action.—Owing to its avidity for water, pure glycerin, when applied to sensitive skin, produces considerable burning and irritation. Internally, in large doses (1 oz.—30 mls), it sometimes acts as a cathartic, probably by abstracting water from the intestinal vessels and also by stimulating peristalsis. In moderate doses glycerin has some nutritive

value, inasmuch as it is largely oxidized in the body and protects from combustion fats and carbohydrates. When large amounts are injected directly into the circulation of an animal they cause muscular weakness, thirst, vomiting, hemoglobinuria, a fall in temperature, a rapid, weak pulse, tetanic convulsions, coma, and finally, death from asphyxia.

Glycerin possesses some power in inhibiting the growth of microorganisms.

Therapeutics.—Externally, glycerin is employed in various forms as an emollient. In the form of an ointment or lotion it is useful in *chapped hands*, *fissured nipples*, etc. It is highly recommended as a preventive against *bed-sores*. The parts should be bathed twice daily with warm water, carefully dried, and gently rubbed with the glycerin. The thorough application of glycerin to the toes and soles of the feet before the stockings are put on is sometimes effective in *bromidrosis*. The official cataplasm of kaolin is a paste of white clay and glycerin. Applied hot, it often makes a good *substitute for the ordinary poultice*. In *endometritis*, *uterine congestion*, and *subinvolution* tampons holding glycerin and tannin afford an efficient means of securing local depletion. In the form of a suppository or of an injection (2-3 fl. dr.—8.0-11.0 mils—with 1-2 fl. oz.—30.0-60.0 mils—of water) it is often employed with advantage to unload the bowel in *simple constipation*.

In *diabetes* glycerin may be employed as a sweetening agent instead of sugar, but, as a rule, patients soon tire of it.

In pharmacy glycerin is extensively used as a solvent, an excipient, and a preservative.

Incompatibles.—Glycerin is explosive with powerful oxidizing agents, such as chromic acid and potassium permanganate. Undiluted mixtures of potassium chlorate, tincture of ferric chlorid, and glycerin are liable to explode if warmed.

TALCUM PURIFICATUM, U. S. P.

(Purified Talc, Venetian Talc, Magnesium Silicate, Soapstone)

Purified talc is a fine white powder, odorless, tasteless, and free from grittiness and slippery to the touch.

It is employed as a dusting-powder in inflammatory diseases of the skin, especially in *erythema intertrigo* and *acute erythematous eczema*. It is usually prescribed with an antiseptic and an adsorbent, as in the following formula:

R̄. Pulveris talci.....	℥iv (15.5 gm.)
Pulveris acidi borici.....	℥j (4.0 gm.)
Pulveris zinci oxid.....	℥iij (11.5 gm.).—M.

KAOLINUM

(Hydrated Aluminum Silicate)

Kaolin is a white, impalpable powder, unctuous when moist. Like talc, it is inert and unalterable. It is used as a protectant in *inflammatory skin diseases*, sometimes as a dusting-powder, but more often in the form of a paste, when ointments and lotions are found to be irritating. Mixed with glycerin, as in the cataplasm of kaolin, and applied hot, it is employed as a *substitute for poultices*. In pharmacy it is used as a *pill-basis* for substances readily decomposed, such as silver nitrate and potassium permanganate.

As a physical adsorbent, it has been recommended by Hektoen, Rappaport, and others as a *means of eliminating diphtheria bacilli from the nose and throat of carriers*. The applications are made three times daily with a powder blower. The results, however, have not been entirely satisfactory. Fullers' earth, a substance closely related to kaolin, but with greater adsorptive power, has been used with some success in the treatment of *diarrhea*. The dose is about 1 dram (4.0 gm.), mixed with water, three or four times a day. It has also been recommended as an antidote in various *alkaloidal poisonings*.

LYCOPODIUM, U. S. P.

Lycopodium is the spores of *Lycopodium clavatum*, a moss growing in the dry woods of nearly all temperate countries. It is a fine, pale-yellowish powder, mobile, inodorous, and tasteless. It is employed in therapeutics chiefly as a protective and adsorbent application to *excoriated surfaces*. In pharmacy it is much used to prevent the adhesion of pills, suppositories, etc.

COLLODIUM, U. S. P.

(Collodion)

Collodion as a solution of pyroxylin, or gun-cotton (4), in ether (75) and alcohol (25). It is a colorless, syrupy, highly inflammable liquid, having a strong ethereal odor.

PREPARATIONS

Collodium Flexile, U. S. P. (collodion, 95; camphor, 25; castor oil, 3)

Collodium Cantharidatum, U. S. P. (Blistering Collodion: Cantharides, 60; flexible collodion, 85; glacial acetic acid, 5; acetone, to make 100.

Therapeutics.—Collodion was introduced into surgery by Schoenbein, in 1846. When applied to an exposed part it

quickly dries and forms a thin film, which in shrinking exerts a constricting and compressing effect. It makes a useful protective for *abrasions*, *fissures*, and *aseptic punctures*. It also affords an efficient means of securing antiseptic dressings on small wounds, especially those about the face and scalp. Flexible collodion makes less pressure and cracks less readily than plain collodion. With the addition of a little benzoin it makes an excellent application for *fissured nipples*, *chapped hands*, etc. A mixture of plain collodion and flexible collodion is sometimes employed as a vehicle for such drugs as chrysarobin, pyrogallol, resorcin, etc., in the treatment of certain skin diseases, especially psoriasis, chronic eczema, lupus erythematosus, and ringworm.

Cantharidal collodion is employed to produce vesication (see p. 482).

LIQUOR GUTTA-PERCHÆ

(Solution of Gutta-percha, Traumaticin)

Solution of gutta-percha is a 9 per cent. solution of gutta-percha in chloroform. It has been used as a substitute for collodion, but it possesses no advantages over the latter.

FLAVORING AGENTS AND VEHICLES

LIMON

(Lemon)

Lemon is the ripe fruit of *Citrus Limonum*, a tree cultivated in most subtropical countries. The rind contains a *volatile oil*, and the juice, *citric acid*.

PREPARATIONS

DOSE

Limonis Cortex, U. S. P.	
Limonis Succus.....	1-2 fl. oz. (30.0-60.0 mls)
Oleum Limonis, U. S. P.....	1-5 min. (0.06-0.3 mls)
Tinctura Limonis Corticis, U. S. P.....	½-1 fl. dr. (2.0-4.0 mls)
Acidum Citricum, U. S. P.....	5-15 gr. (0.3-1.0 gm.)
Syrupus Acidi Citrici, U. S. P. (1 per cent.)..	1-4 fl. dr. (4.0-15.0 mls).

The oil of lemon also enters into compound spirit of orange, compound spirit of ammonia, and aromatic elixir.

Therapeutics.—Lemon-juice is especially useful in *scurvy*, both as a preventive and a curative agent. In the form of lemonade, it makes a pleasant refrigerant drink in *febrile diseases*.

Hamm, Somers, and others have found citric acid of value in preventing the fetid odor of *atrophic rhinitis*. A powder composed of 1 part of the acid with 3 parts of sugar-of-milk is insufflated into the nostrils two or three times daily after the parts have been thoroughly cleansed with an alkaline solution.

All the preparations of lemon are largely used for flavoring purposes.

AURANTIUM

(Orange)

Two varieties of the orange furnish the materials for the official preparations: Bitter orange (*Citrus Aurantium amara*) and sweet orange (*Citrus Aurantium sinensis*).

PREPARATIONS	DOSE
Aurantii Amari Cortex, U. S. P.....	15-30 gr. (1.0-2.0 gm.)
Fluidextractum Aurantii Amari, U. S. P.....	10-20 min. (0.6-1.2 mls)
Tinctura Aurantii Amari, U. S. P.....	½-1 fl. dr. (2.0-4.0 mls)
Aqua Aurantii Florum, U. S. P.....	Indefinite
Aqua Aurantii Florum Fortior, U. S. P.	
Syrupus Aurantii Florum, U. S. P.....	Indefinite
Aurantii Dulcis Cortex, U. S. P.....	15-30 gr. (1.0-2.0 gm.)
Tinctura Aurantii Dulcis, U. S. P.....	½-1 fl. dr. (2.0-4.0 mls)
Syrupus Aurantii, U. S. P.....	Indefinite
Oleum Aurantii, U. S. P. (expressed from the fresh peel of sweet orange).....	1-5 min. (0.06-0.3 mil)
Spiritus Aurantii Compositus, U. S. P. (oil of orange, 20; oil of lemon, 5; oil of cori- ander, 2; oil of anise, 0.5; deodorized alcohol, to make 100).....	1-2 fl. dr. (4.0-8.0 mls)
Elixir Aromaticum, U. S. P. (compound spirit of orange, 12; syrup, 37.5; alcohol and water, to make 100).....	1-2 fl. dr. (4.0-8.0 mls).

Bitter orange-peel also enters into compound tincture of cinchona and compound tincture of gentian.

Therapeutics.—Bitter orange-peel is a feeble stomachic; but, like the sweet orange, it is employed almost exclusively as a flavoring agent.

ERIODICTYON, U. S. P.

(Yerba Santa)

Eriodictyon is the leaves of *Eryodictyon californicum*, an evergreen shrub growing in California. It contains tannin, an acrid, bitter resin, and a trace of volatile oil.

PREPARATIONS

DOSE

Fluidextractum Eriodictyi, U. S. P.....	10-20 min. (0.6-1.2 mls)
Syrupus Eriodictyi Aromaticus (fluidextract, with compound tincture of cardamom, oil of sassafras, oil of lemon, oil of cloves, potassa solution, alcohol, and syrup).....	1-2 fl. dr. (4.0-8.0 mls).

Uses.—Eriodictyon has been used to some extent as a stimulant expectorant; it is chiefly valuable, however, in the form of the aromatic syrup, to obtund the bitterness of quinin. The aromatic syrup is incompatible with acids.

SARSAPARILLA, U. S. P.

Sarsaparilla is the root of *Smilax officinalis* and of other species of *Smilax*, climbing evergreens growing in swampy forests in Central and South America. It contains several glucosids of the *saponin* class.

PREPARATIONS

DOSE

Fluidextractum Sarsaparillæ, U. S. P.....	½-1 fl. dr. (2.0-4.0 mls)
Fluidextractum Sarsaparillæ Compositum, U. S. P. (sarsaparilla, 75; glycyrrhiza, 12; sassafras, 10; mezereum, 3; with glycerin, 10; alcohol and water, to make 100).....	½-1 fl. dr. (2.0-4.0 mls)
Syrupus Sarsaparillæ Compositus, U. S. P. (fl. ext. sarsaparillæ, 20; fl. ext. glycyrrhiza, 1.5; fl. ext. senna, 1.5; oil of sassafras, oil of anise, methyl salicylate, of each 0.02; alcohol, 1.9; syrup to make 100).....	1-4 fl. dr. (4.0-15.0 mls).

Uses.—Sarsaparilla has been employed for more than three hundred years as an alterative in *syphilis* and *tuberculosis*, but its beneficial effects in these diseases are very doubtful. It is chiefly useful in the form of the compound syrup as a vehicle for potassium iodid and soluble mercurial salts.

SASSAFRAS, U. S. P.

Sassafras is the bark of the root of *Sassafras variifolium*, a shrub or tree growing in the woods of North America. It contains a volatile oil, *Oleum Sassafras*, U. S. P., the dose of which is from 1 to 5 minims (0.06-0.3 mil).

Sassafras enters into the compound fluid extract of sarsaparilla and the compound syrup of sarsaparilla.

LAVANDULA

(Lavender)

Lavender is the flowers of *Lavandula officinalis*, a shrub indigenous in southern Europe. It contains volatile oil, tannin, and resin.

PREPARATIONS

DOSE

Oleum Lavandulæ Florum, U. S. P.	1-5 min. (0.06-0.3 mil)
Spiritus Lavandulæ, U. S. P.	½-1 fl. dr. (2.0-4.0 mls)
Tinctura Lavandulæ Composita, U. S. P. (oil of lavender, with oil of rosemary, cinnamon, cloves, nutmeg, and red saunders)	½-1 fl. dr. (2.0-4.0 mls).

Uses.—The preparations of lavender are used solely for their agreeable flavor.

The compound tincture is an ingredient in Fowler's solution.

ROSA

(Rose)

Rose is official as the dried petals of *Rosa gallica*, a species of red rose largely cultivated in western Asia and southern Europe. The chief constituents are a volatile oil, tannin, sugar, and mucilage. The official oil of rose is distilled from the fresh flowers of the Damascus rose (*Rosa damascena*).

PREPARATIONS

Fluidextractum Rosæ, U. S. P.	
Mel Rosæ, U. S. P. (12 per cent. of fluidextract in clarified honey)	
Aqua Rosæ Fortior, U. S. P. (water saturated with oil of rose)	
Aqua Rosæ, U. S. P. (stronger rose-water and distilled water, equal volumes)	
Unguentum Aquæ Rosæ, U. S. P. (stronger rose-water, 19; expressed oil of almond, 56; spermaceti, 12.5; white wax, 12; borax, 0.5).	

Uses.—The liquid preparations of rose are used as agreeable vehicles. Ointment of rose-water (cold cream) is used as an emollient and as a basis for other ointments.

SACCHARUM, U. S. P. AND SACCHARUM LACTIS, U. S. P.

(Cane-sugar or Sugar and Sugar-of-milk or Lactose)

Cane-sugar is the refined sugar from sugar-cane (*Saccharum officinarum*), from various species of broom-corn (*Sorghum*), and from one or more varieties of sugar-beet (*Beta vulgaris*).

PREPARATION

Syrupus, U. S. P.

Cane-sugar also enters into the various compound syrups, the various troches, several mixtures, and numerous other preparations. It is employed exclusively as a sweetening agent, a preservative, and a vehicle or excipient.

Sugar-of-milk is the sugar obtained from the whey of cow's milk. It is harder, less soluble, and less sweet than cane-sugar. It is used largely as a diluent for powders. It has some merit also as a diuretic in cardiac dropsy.

LEVULOSE

(Fruit-sugar, Fructose)

Levulose is a saccharine substance found in most sweet fruits, together with grape-sugar, and prepared artificially by hydrolysis from cane-sugar or from inulin, a starchy body contained in inula or elecampane. It occurs as a thick, syrupy liquid or as a coarse, granular powder, and is almost as sweet as cane-sugar. It was recommended by Kütz, in 1874, as a sweetening agent and as a carbohydrate food in diabetes.

BENZOSULPHINIDUM, U. S. P.

(Benzosulphinid, Saccharin, $C_6H_4SO_2.CONH$)

Saccharin is a principle prepared from the coal-tar derivative, toluene. It is a light, white, crystalline powder, odorless, and possessing 400 to 500 times the sweetening power of cane-sugar. It is soluble in 290 parts of water, more so in alcohol and in glycerin, and readily so in alkaline solutions. With solution of sodium bicarbonate it forms a soluble sodium salt, *soluble saccharin*. Saccharin is chiefly useful as a substitute for sugar when the latter is contraindicated, as in diabetes mellitus. Used too freely, it has a retarding influence on digestion and general metabolism. The ingestion of $3\frac{1}{2}$ drams (14.0 gm.) of soluble saccharin, equal to about 1 dram (3.5 gm.) of free saccharin, resulted in dizziness, delirium, vomiting, and an extensive erythematous and bullous eruption, but not in death. One grain (0.065 gm.) is sufficient to sweeten 4 or 5 ounces (120.0–150.0 mls) of tea or coffee.

MEL, U. S. P.

(Honey)

Honey is a saccharine fluid prepared by the hive-bee (*Apis mellifera*). It is a mixture of dextrose (grape-sugar) and levulose (fruit-sugar), with minute quantities of wax, formic acid, volatile oil, and coloring-matter.

PREPARATIONS

Mel Depuratum, U. S. P. (clarified honey)

Mel Rosæ, U. S. P.

Uses.—Honey is demulcent and feebly laxative, but it is prescribed chiefly as an excipient.

Wild cherry, licorice, balsam of Tolu, and many volatile oils are also largely used for flavoring purposes.

REMEDIAL MEASURES OTHER THAN DRUGS

ELECTRICITY

Electricity, like the other great forces in nature, must be studied in the light of its various manifestations. Gilbert first employed the term to designate the phenomena of attraction and repulsion which result when amber (electrum) and similar substances are briskly rubbed. Electricity produced in this simple way—by the rubbing together of certain substances—is termed **frictional or static electricity or franklinism**.

When two dissimilar metals, such as copper and zinc, are placed in a corrosive fluid and united outside by a loop of wire, the resulting chemical action is attended with the production of an electric current, and to this manifestation of electricity the term **galvanism** is applied. The vessel, its contained fluid, and connected elements together constitute a *galvanic cell*. The union of several cells forms a *battery*. The energy which starts the electric current is termed the *electromotive force*, and it is always the same in quantity for the same materials at the same temperature, and is entirely independent of the size and shape of the plates and of the distance between them. The current is generated at the surface of the element or plate more easily corroded, which in the above illustration is the zinc, and passes through the fluid to the element or plate less affected—that is the copper—and from the external end of the copper it passes through the wire loop back again to the external end of the zinc, thus completing a *closed circuit*. As the external end of the copper is constantly giving off electricity, it is termed the *positive pole*, or *anode*; and as the external end of the zinc is constantly receiving electricity, it is termed the *negative pole*, or *cathode*.

It is evident that the electromotive force will more than represent the strength of the current, for all substances offer more or less resistance to the passage of electricity. The resistance within the cell is termed the *internal resistance*, and that without the cell the *external resistance*. The amount of internal resistance will depend upon the character of the intervening fluid, the size of the plates, and their proximity. The larger the plates and the closer they are to each other, the less becomes the internal

resistance. The external resistance depends upon the length, diameter, and character of the conductor. The law of the relation of the *current-strength* to the electromotive force and to the resistance was discovered by Ohm, in 1827: *The strength of an electric current passing a section of the conductor in a unit of time is proportional to the whole electromotive force, and inversely proportional to the sum of all the resistances in the circuit.* Representing the current-strength by C , the electromotive force by E , the internal resistance by Ir , and the external resistance by Er , the law may be expressed by the following formula:

$$C = \frac{E}{Er + Ir}.$$

The unit of resistance is termed an *ohm*; the unit of electromotive force, a *volt*; and the unit of current-strength, an *ampere*. As the last is too large a unit for medical purposes, $\frac{1}{1000}$ of an ampere, or a *milliampere*, is employed instead.

An electromotive force of one unit acting upon a conductor offering one ohm of resistance will set up in that conductor a current of one ampere.

The current-strength of a battery can be increased in three ways: (1) by diminishing the external resistance; (2) by diminishing the internal resistance; and (3) by increasing the number of cells. When the external resistance is a fixed quantity, which is often the case, the current-strength can still be increased in one of the two remaining ways; but when the external resistance is very great, as in the case of the human body, in which it is about 3000 ohms, the gain secured by enlarging the plates and lessening the distance between them is but trifling, and the current-strength must, therefore, be increased by multiplying the number of cells.

When the external resistance is slight, as in the galvanocautery, in which the current has only to render a piece of wire incandescent, the internal resistance becomes highly important, and much is gained by reducing it to a minimum. It follows, therefore, that a battery designed for such a purpose should consist of a few cells with large plates placed very near one another. The same principles likewise apply to the construction of batteries intended for electrolytic work.

Both galvanic and faradic currents may also be derived from *dynamoes* used in producing electricity for commercial purposes.

Of the accessories to a battery, the most important are the galvanometer, rheostat, and electrodes.

A galvanometer is an instrument for measuring the current-strength.

A rheostat, or resistance-coil, is an appliance for placing in the circuit a known resistance; by it the external resistance can be increased to any extent and kept uniform.

Electrodes are appliances of various sizes and shapes placed at the pole-ends so that the current can be conveniently transferred to the body.

Faradism, or Induced Electricity.—This manifestation of electric force depends upon the power which a galvanic current possesses, while passing through one conductor, of inducing momentarily a current in an overlying conductor. The induced current is instantaneous, and appears only at the making or breaking of the galvanic current. Moreover, it flows in a direction opposite to that of the galvanic current when the latter is made, and in the same direction when it is broken. By rapidly making and breaking the primary current a powerful to-and-fro current is induced in the overlying conductor. A faradic battery consists of cells for generating the galvanic current; a *primary coil*, consisting of a few turns of coarse insulated wire inclosing a coil of soft iron; a *secondary coil*, composed of many turns of very fine wire surrounding the primary coil, but not touching it; and a mechanical device for slowly or rapidly making or breaking the current in the primary circuit.

The current derived from the primary coil is termed the *primary current*; like the galvanic, it flows in one direction and affords a positive and a negative pole. It differs, however, from the galvanic current in being reinforced by the turns of the coil. The current derived from the secondary coil is termed the *secondary current*, and, since it is ever changing the direction of its flow, it cannot furnish negative and positive poles.

The **sinusoidal current** is an alternating current with a gradual change of strength and direction. Its name is derived from the sinusoidal curve that is formed by a graphic record of the current.

High-frequency currents, or currents with an extremely high rate of oscillations per second, may be obtained from static machines or induction coils by various forms of apparatus. Three types of these currents, differing from one another in physical character, are employed: D'Arsonval, Oudin, and Tesla currents. The D'Arsonval current, which is of low voltage and of relatively high amperage, is employed for its constitutional effects; the Oudin and Tesla currents, which are of high voltage and comparatively low amperage, are used chiefly for their local and reflex effects.

Physiologic Effects of Electricity.—The **Static Current**. Static sparks when applied singly to a motor point cause muscular contractions. A stream of static sparks applied to one spot

causes redness and pain, followed by blanching and numbness. Prolonged, powerful applications may produce a superficial escharotic effect. The static current is also capable of exerting a profound psychic effect.

The Galvanic Current.—The galvanic current is capable of causing local congestion, stimulating muscular contractions, producing electrolytic and chemical effects, and influencing osmosis. When a powerful uninterrupted galvanic current is applied to sensitive parts of the body through moistened electrodes, it produces at the points of contact severe burning pain, redness, and, finally, under the negative pole, vesication. These phenomena are the result of electrolytic changes induced by the current. When the circuit is broken and again when it is closed active muscular contraction occurs; in the interval between opening and closure, however, the muscle is quiescent.

When the negative pole, or cathode, is placed over the nerve supplying a healthy muscle, and the positive pole, or anode, over some indifferent point, as the sternum, and a weak current is used, a contraction of the muscle occurs on closing the circuit, but none on breaking it. When the positive pole is placed over the nerve and the negative over the sternum, and a somewhat stronger current is employed, a contraction occurs when the circuit is broken. With a still stronger current a contraction occurs also when the circuit is closed. When the negative pole is over the nerve, contractions on breaking the circuit occur only with currents of very great power.

The following table represents the relative strengths of the various contractions in normal muscles, 1 being the strongest:

1. Cathodal closing contraction (CaClC).
2. Anodal opening contraction (AnOC).
3. Anodal closing contraction (AnClC).
4. Cathodal opening contraction (CaOC).

When one pole is placed over the sternum and the other over the *motor point* of the muscle—i. e., the point of entrance of its motor nerve—contractions are obtained with weaker currents and the reactions are somewhat changed, the anodal closing contraction becoming stronger than the anodal opening contraction.

Effect of the Faradic Current.—The faradic current acts as an irritant, causing excitation of sensory nerves, vasodilation, and contraction of healthy muscles. When a strong induced current is applied to a part, it causes a tingling sensation, followed by numbness. If a dry metallic electrode be used, the contact excites severe pain. When the current is passed directly

through a muscle, it causes a continuous or tetanic contraction which lasts until the current ceases to flow.

The Reaction of Paralyzed Muscles to Electric Currents.—When a galvanic current is applied to a paralyzed part, the reactions may be normal, they may be altered quantitatively, *i. e.*, increased or diminished—or they may be altered qualitatively.

A normal response of the muscles to both galvanic and faradic currents often occurs in hysteric paralysis and in paralysis of cerebral origin. An increased response to both currents without qualitative change indicates a state of irritation or hypersensitivity of the spinal centers or peripheral nerves, and may be observed very early in apoplectic hemiplegia, very early in neuritis, and in some cases of hysteria. A diminished response to both currents without qualitative change is observed in pseudomuscular hypertrophy, in progressive muscular atrophy until a late period of disease, and sometimes in neuritis after the very early stage, and before much degenerative change has taken place in the nerve-trunk or muscles.

Reaction of Degeneration (DeR).—This consists in a qualitative change in the electric reaction, a reversal of that occurring in normal muscle. It is obtained only with the *galvanic current* when the electrode is placed over the *muscle*—not its motor nerve or motor point—and is observed in paralyzed muscles which are in certain stages of degeneration on account of a lesion of their supplying nerves or of that portion of the spinal cord from which those nerves have their origin; or, in other words, when the muscles are cut off from the trophic influences which emanate from the ganglionic cells in the gray matter of the spinal cord. In such cases the muscles fail to respond to the faradic current, but still respond to the galvanic current. The responses, however, instead of being immediate and short as in health, are sluggish and persistent, and, moreover, are reversed in their sequence. Thus, the anodal closing contraction may equal, or at a later period may exceed, the cathodal closing contraction, and the cathodal opening contraction may equal or exceed the anodal opening contraction. These reactions may be expressed as follows:

AnClC equals or is greater than CaClC.

CaOC equals or is greater than AnOC.

The Sinusoidal Current.—This current has the same physiologic properties as the faradic current, but has the advantage of producing little or no pain.

High Frequency Currents.—These currents have a heating effect, increase metabolism, and dilate the peripheral vessels,

thus lowering arterial tension. Locally, they may have no effect on the skin, or, according to the strength of the application, they may cause redness and even destruction of tissue. Usually, they do not excite muscular contractions.

Secondary Effects of Electricity.—The secondary effects of electricity—heat, light and x-ray and other radiations—have physiologic actions which make them useful in the treatment of many different conditions.

Therapeutics.—Electricity is employed in medicine to restore the functional activity of the muscles in palsies of peripheral origin; to combat various sensory disturbances, which are of a functional nature or which depend upon minor lesions of the peripheral nerves or their centers; to influence metabolism and improve general nutrition; to arouse the nerve-centers in states of profound depression; to lower the bloodpressure in hyperpiesis; to produce counterirritation, to favor the absorption of inflammatory exudates or degenerative products; to effect the rapid absorption of drugs through the unbroken skin (cataphoresis); to bring about the coagulation of blood in aneurysmal sacs; and, in the form of the galvanocautery and high frequency current, to destroy papillomas, epitheliomas, superfluous hair, etc.

Whether the good achieved by electricity in certain functional nervous disorders, such as hysteria, hypochondriasis, etc., is to be ascribed to the specific action of the electricity itself, or is to be regarded as being wholly the result of suggestion, is a question upon which opinion is divided. It cannot be denied, however, that in many instances, at least, the benefit obtained is mainly a psychic effect.

In *paralysis from lesions of the peripheral nerves*, if the damage to the nerve has not been too great, much benefit may often be derived from the use of electricity. Applications should not be made, however, until all symptoms of irritation have subsided. The faradic current may be used if the muscles respond to it, one electrode being placed over the motor nerve or the motor point of the muscle, and the other over some indifferent place, such as the back or chest. In the more severe cases in which faradic excitability is lost the galvanic current should be employed, the negative electrode being applied to the motor nerve or to the muscle, and a current of 4 to 8 milliamperes allowed to flow for about 5 minutes.

In *acute poliomyelitis* electric treatment, carried out for from 6 months to a year or more, is a valuable adjuvant to light massage and passive movements in restoring power to certain groups of muscles, but it must not be instituted until all tenderness has disappeared, which may not be for from 6 to 8 weeks or more.

The faradic current should be employed if it produces contractions, otherwise the galvanic current should be selected. The treatment should be carried out systematically for 10 or 15 minutes daily, using only such strength of current as will produce moderate contractions without pain. The use of the sinusoidal current has also been highly praised.

In *hemiplegia* from cerebral hemorrhage, thrombosis or embolism, in *chronic poliomyelitis* and in *primary muscular dystrophy* electricity is of no value. In *locomotor ataxia*, while electricity exerts no influence on the progress of the disease, it is sometimes of service in the form of the galvanic current, faradic brush or sinusoidal current, in relieving lancinating pains and paresthesia. J. K. Mitchell found faradism beneficial also in rectal and vesical tenesmus.

In so-called *idiopathic neuralgia* electricity, in the form of the stabile or labile galvanic current, high frequency current, or static sparks, may afford some relief. When the galvanic current is employed the anode should be placed, as a rule, peripherally and the cathode at some indifferent spot. Temporary alleviation of pain can be secured also by cataphoresis. A satisfactory method is to cover the positive pole with several layers of tissue-paper wet with a 10 per cent. solution of cocain and to apply it over the most painful spot. With a current of from 5 to 10 milliamperes local anesthesia can be induced in about 5 minutes. A lasting counterirritant effect, if this is desired, can be produced with ultraviolet rays.

Electricity is sometimes useful in *myalgia*. It may be applied in the form of faradization, one sponge electrode being placed over an indifferent spot and the other rubbed over the painful area, in the form of heavy galvanic currents, or in the form of high-frequency currents from the d'Arsonval transformer. Salicylic ionization may also be used. The negative electrode (a large one) is moistened with a 4 per cent. solution of sodium salicylate and applied to the seat of pain, the other electrode is applied a few inches away, and a current gradually increased to 50 milliamperes or more is applied for half an hour.

In *primary neurasthenia* faradic applications, using a weak current with rapid interruptions, galvanic applications, with a current of 2 to 4 milliamperes and a large negative electrode applied to the feet and a positive electrode rubbed over different parts of the surface, or high-tension high-frequency currents, may be a useful adjuvant to other therapeutic measures. In *hysteria* electricity is sometimes efficacious, probably through its psychic effect, in dispelling certain local symptoms, particularly anesthesia, paresthesia, and pain. Faradization with the wire brush

and static-spark applications are the forms most generally useful. In hysteric paralysis, electricity, especially faradic and galvanic applications, sometimes proves harmful rather than beneficial by fixing the patient's attention upon her condition, thus tending to perpetuate it. General faradization forms a part of Weir-Mitchell treatment of hysteria, which is especially applicable to refractory cases.

Exophthalmic goiter is sometimes benefited by galvanic treatment systematically carried out. The best results are obtained with weak currents, the cathode being placed over the neck near the angle of the lower jaw, while the anode is applied to the opposite side next to the lower cervical vertebræ. The applications should be made daily, and each should be short, lasting not longer than from 3 to 5 minutes.

According to Barton Cooke Hirst, excellent results are often obtained in *infantile uteri*, whether congenital or due to superinvolution, from the systematic use of negative galvanism.

In *asphyxia by coal gas* and in *poisoning by opium and other narcotics* strong rhythmic faradic shocks afford an efficient means of arousing the patient without increasing exhaustion or causing any other ill effects.

High frequency currents are of some value in reducing the bloodpressure in cases of *high arterial tension*, but the effect is only temporary, unless other therapeutic measures are coincidentally employed.

The method of treating *aneurysms of the aorta* by means of fine wire introduced through a hollow needle or cannula and coiled within the sac was first suggested by Charles H. Moore, in 1864. Corradi, in 1879, demonstrated that the procedure could be made more effective by passing a strong galvanic current through the wire after it has been inserted into the aneurysm, thus producing more rapid and more firm coagulation. The treatment is safe when performed by an experienced operator and often yields very satisfactory results, almost always relieving pain and in some cases apparently prolonging life. It is only suitable, however, for aneurysms of the sacculate variety and should never be attempted in fusiform aneurysms. The technique of the procedure is briefly as follows: After the skin has been sterilized, an insulated hollow needle or cannula is inserted into the aneurysm where the sac wall seems nearest to the surface, and through this from 10 to 40 (300–1200 cm.) feet of fine gold or platinum-gold wire are introduced into the sac. The external end of the wire is now connected with the positive pole of a galvanic battery and the current is completed by the application of a large wet electrode, attached to the negative pole, under the patient's back. Begin-

ning with 5 milliamperes, the current is increased by 5 additional milliamperes every 5 minutes until 50 milliamperes are reached and then the current is gradually reduced. At the end of from 30 minutes to an hour the electrodes are disconnected, the needle is withdrawn, the free end of the wire is fixed beneath the skin and the puncture is sealed. After the operation the patient should remain in bed for a period of 2 or 3 weeks so that the clot shall become thoroughly consolidated. An anesthetic is required for aneurysms of the abdominal aorta, but not for aneurysms of the thoracic aorta. In 25 cases reported by Hare there were no accidents and benefit was secured in all.

Electrodesiccation, produced by a monopolar high-frequency current of the Oudin type, and electrocoagulation, produced by a bipolar high-frequency current of the d'Arsonval type, are of value in destroying benign or malignant growths of small or moderate size in accessible regions. These electrothermic methods have been found especially useful in the treatment of *moles, nevi, tattoo marks, angiomas, papillomas, lupus, leukoplakia, and epitheliomas of the skin, mouth, tongue, larynx, proximal end of the esophagus, and bladder*. Electrocoagulation has a more powerful and a more penetrating effect, and is utilized in destroying somewhat larger growths involving the deeper tissues, including bone. The galvanocautery is also often used to destroy pathologic tissue, such as so-called *nasal hypertrophies* and *patches of lupus*. Electrolysis is a reliable method of removing permanently *superfluous hair* and *ingrowing eyelashes*.

MASSAGE

The term massage is applied to systematic stroking, kneading, rubbing, and percussion of the body. One who practises massage is known as a *masseur*, if a male, and as a *masseuse*, if a female.

Effleurage, or stroking, consists in slowly drawing the flat of the hand or the finger-tips over the surface of the body in the direction of the venous circulation. Very slight pressure should be made in the movements. *Effleurage* stimulates the cutaneous nerves and quickens the lymphatic and venous circulations.

Pétrissage, or kneading, is performed by grasping the tissues between the palmar surfaces of the hands, between the fingers and thumb, or between the finger-tips only, raising them slightly, and then rolling them while alternately tightening and relaxing the hold. Kneading serves to remove waste-products from the tissues, stimulates the circulation, and promotes nutrition.

Friction, or rubbing, is done by making circular movements, under some pressure, with the palm of the hand or the fingertips, the up-stroke being heavy and the down-stroke light. The movements should always be centripetal. Friction exerts about the same influence on the tissues as kneading.

Tapotement, or percussion, consists in delivering, with the palm of the hand, the ulnar surface of the hand, or the tips of the fingers, rapid rhythmic blows. Palmar percussion is used chiefly on the limbs; ulnar percussion on the chest and back; and digital percussion on small uneven surfaces like the face. Percussion acts as a nerve and muscle stimulant.

General Massage.—When general massage is to be practised, the operator begins at one extremity, generally a leg, and applies to each in turn friction, kneading, palmar percussion, and palmar stroking. After the limbs, the chest receives friction, kneading, ulnar percussion, and palmar stroking. Next the abdomen is treated, deep friction and kneading being applied over the entire surface, and palmar stroking along the course of the ascending, transverse, and descending colon. Finally, vigorous stroking is applied over the spine from above downward, and the muscles of the back are subjected to friction, kneading, and ulnar percussion. In some cases various movements, such as flexion, extension, circumduction, etc., intended to secure passive exercise of the muscles, are a valuable adjuvant to general massage.

Generally, massage is best given in the forenoon, about an hour after breakfast. It should never be given on an empty stomach. At first the séances should not last more than 15 or 20 minutes, but later they may be extended with advantage to an hour. To secure the best results the operation should be repeated daily. The patient should be recumbent and loosely wrapped, so that the hands of the operator may be applied directly to the skin. The room should be free from drafts, and the temperature of the atmosphere about 70° F. (21.1° C.). After the treatment the patient should be warmly covered and left to rest for from twenty minutes to an hour.

Unless the patient's skin is very harsh and dry or is unduly sensitive, the masseur need not use a lubricant for the hands; if, however, one is desired, cocoanut oil or cold cream is probably the best.

The effects of general massage in individuals who are required to be at rest are much the same as those of active exercise in persons who are able to be about. Thus, the immediate effects are a sense of tiredness without exhaustion and an agreeable feeling of drowsiness. The general circulation is first quickened

and then slowed, the waste-products are squeezed out of the tissues, and the activity of the lymph-flow is increased. Later, massage whets the appetite, favors digestion, tends to secure restful sleep, stimulates metabolic activity, and promotes general nutrition.

Therapeutics.—In the *paralysis* following *cerebral hemorrhage*, *acute poliomyelitis*, and *neuritis* massage is of value in maintaining the nutrition of the affected muscles; even when power is hopelessly lost, it tends to retard the development of contractures. Mechanical treatment, however, should not be instituted in these cases until all signs of irritation have subsided. In *neuralgia* and *sciatica* local massage is a useful adjuvant to other measures.

Massage is believed to be of some benefit in maintaining the nutrition of the muscles in *progressive muscular atrophy*, *amyotrophic lateral sclerosis*, and *chronic myelitis*.

Writers' cramp and other *occupation spasms* are best treated by rest, hot and cold douches, galvanism and local massage.

In *sprains* rapid relief is afforded by soaking the part in hot water for half an hour, then practising massage, and subsequently applying a firm bandage. The treatment should be instituted immediately after the accident. For the first 10 or 15 minutes the massage should consist of light digital stroking applied in a centripetal direction above and below the affected joint, the latter not being touched; after this, however, gentle friction may be applied directly to the inflamed tissues. The treatment should be repeated two or three times daily.

Massage is often serviceable in hastening the absorption of inflammatory exudation and in imparting suppleness to the affected joints, in *traumatic arthritis*, *luxations*, *synovitis*, *chronic articular rheumatism*, *chronic gout*, and *rheumatoid arthritis*. In acute rheumatism and acute gout manipulations are contraindicated while the acute symptoms are present.

In *chronic constipation* the result of intestinal atony, abdominal massage systematically practised is a useful adjuvant to other measures.

In *hysteria* and *neurasthenia* passive movements afford a valuable means of securing the benefits of exercise without the expenditure of strength. They are an important element in the Weir-Mitchell treatment, which includes also isolation, the administration of readily assimilable food in large quantities, and electricity. In *chronic heart-disease*, *diabetes*, *obesity*, and *severe anemia*, when the patient is unable to take active exercise, massage is a great help in stimulating metabolic processes and in improving the general nutrition.

Contraindications.—Massage should not be employed in any disease that is attended with fever. In pregnancy abdominal manipulation is contraindicated, although the treatment may be applied to other parts of the body up to the first stage of labor. Inflammatory diseases of the skin and processes attended with suppuration also forbid massage.

MOVEMENT THERAPY FOR LOCOMOTOR ATAXIA

The treatment of locomotor ataxia by exercises intended to reëducate the muscles to perform coördinated movements, first described by Frenkel in 1890, has won for itself the support of many distinguished neurologists. Properly carried out, it may serve to keep patients on their feet for several years, when otherwise they might become bedridden, or it may serve even in getting them about again when they have been unable to walk for a long period, perhaps many months.

For exercising the upper extremities the following directions are given: Sit in front of a table, place the hand upon it, then elevate each finger as far as possible; raising the hand slightly, extend and then flex each finger and thumb as far as possible; do this with the right and then with the left hand. Touch with the end of the thumb each finger-tip separately and accurately; then touch the middle of each phalanx with the tip of the thumb. Sit at the table with a large sheet of paper and a pencil; make a dot at each corner of the paper and one in the center, and draw lines from the corner dots to the center dot, first with one hand and then with the other. Put ten coins on the paper, pick them up, and place them in a single pile, first with the right and then with the left hand.

For the body and legs, the following are sample exercises: Sit in a chair, rise slowly to erect position without the help of cane or arms of chair; then sit down slowly; stand with cane, feet together; advance left foot and return it with exactness to original position; then the same with right foot. Walk slowly ten steps forward and five back with help of canes. Stand without cane, but with the feet a little apart and the hands on the hips; in this position stoop down by flexing the knees, and rise slowly. Stand without cane with the feet separated; raise the hands from the sides above the head; carry them downward and forward, and try to touch the toes. Walk along a fixed line on the floor by the help of a cane, placing each foot in turn on the line; then repeat without using the cane.

When the patient is confined to bed, the exercises must be taken in a recumbent position. He is required to flex, extend,

abduct, and adduct each leg separately and then both simultaneously. He is asked to place the heel of one foot on the big toe of the other foot, and then on various points from the ankle to the knee. He may be called upon to follow alternately, first with one foot and then with the other, lines drawn upon a small blackboard placed at the foot of the bed (Rhein).

To secure good results from Frenkel's treatment, the following points should be borne in mind: The exercises must not be applied in a routine manner; they should be carefully adapted to the particular needs of each patient. Each movement should be made slowly and deliberately, with the greatest possible exactitude, and repeated three or four times, first with the eyes open and then with the eyes closed. Owing to the benumbing of the sense of fatigue in tabetic patients, great care must be exercised to guard against exhaustion. The séances should not last longer than ten or fifteen minutes, and at first no more than two should be allowed a day. After the exercises the patient should lie upon his back until completely rested. Gymnastics of all kinds are to be forbidden during the treatment. For the first week or two, at least, the movements should be done under the direct supervision of the physician himself or a trained assistant. The duration of the treatment will depend largely upon the degree of the motor disturbances present, but in any case it should not be less than several months. Even when the exercises appear to be no longer necessary, they should be resumed at frequent intervals.

Contraindications.—According to Frenkel, the treatment is absolutely contraindicated in acute cases. As vision is essential in performing the various movements, blindness is also a contraindication. Raichline further adds that the patient should possess a certain amount of energy and intelligence, that sensation should not be absolutely lost, and that arthropathies and spontaneous fractures should not be present.

THE SCHOTT OR NAUHEIM TREATMENT

The treatment of chronic heart-disease carried out by the brothers Schott at Nauheim, Germany, consists of bathing in natural effervescent baths and of graduated exercises. The waters of Nauheim have a temperature of from 86° to 95° F. (30°–35° C.), and are very rich in carbonic acid and in mineral ingredients, especially sodium chlorid and calcium chlorid. The baths first prescribed have a temperature of from 95° to 90° F. (35°–32° C.), contain about 1 per cent. of sodium chlorid and 0.1 per cent. of calcium chlorid, and are free from car-

bonic acid gas. The patient is directed to remain in the water not more than five or ten minutes. The duration of the baths and their salinity are gradually increased, while their temperature is gradually lowered. Eventually, after the lapse of a week or two, baths containing carbonic acid gas, and about 3 per cent. of sodium chlorid and 0.3 per cent. of calcium chlorid are taken, the temperature of the water being reduced as low as 80° F. (27° C.). After the bath the patient is well rubbed and allowed to rest for an hour.

Artificial baths may be prepared at home in imitation of those at Nauheim. At the beginning of the treatment the bath should contain 1 pound (454.0 gm.) of sodium chlorid and 1½ ounces (45.0 gm.) of calcium chlorid for every 10 gallons (38.0 L.) of water, and the temperature of the water should be from 95° to 90° F. (35°–32° C.).

The baths may be given every other day or every day, their duration being gradually prolonged from five or ten minutes to fifteen or twenty minutes. With the increased duration of the baths their temperature is gradually lowered until a minimum of 80° F. (27° C.) is attained, and their salinity is gradually increased until a maximum of 3 pounds (1360.0 gm.) of sodium chlorid and 4½ ounces (140.0 gm.) of calcium chlorid to every 10 gallons (38.0 L.) is reached.

The plain saline baths are to be followed by effervescent baths. The latter may be prepared artificially by dissolving in the saline baths 2 ounces (60.0 gm.) of sodium bicarbonate for every 10 gallons (38.0 L.) of water, and then adding very slowly 3 ounces (90.0 mls) of hydrochloric acid which has been previously well diluted. The amount of soda and acid may be gradually increased until that of the former reaches a maximum of 8 ounces (245.0 gm.), and that of the latter a maximum of 12 ounces (355.0 c.c.).

A more convenient method of generating the carbonic acid is by using prepared tablets of sodium bisulphate with an acid reaction and powders of sodium bicarbonate.

The effect of the baths is to diminish the pulse-rate, to increase the force and volume of the pulse, to lessen the frequency of the respirations, to increase the secretion of urine, and, in cases of cardiac dilatation, to diminish the area of cardiac dulness. The theory of August Schott is that the good effects of the baths are largely the result of a reflex stimulation of the heart through excitation of the cutaneous nerves.

The exercises consist of a series of simple movements of each limb and of the trunk, which are gently resisted by the hand of the attendant. Massage may also be added to the

gymnastics with good results. It is highly important in carrying out the exercises to avoid fatigue. The slightest suggestion of dyspnea or of cyanosis is to be regarded as a signal for discontinuing the treatment. The effects of the exercises are very similar to those produced by the baths. It has been suggested that these effects are also brought about reflexly, a centripetal influence being exerted by the muscular contractions upon the ganglionic centers of the heart.

Broadbent, however, is of the opinion that "the baths or resisted movements give rise to a physiologic dilatation of the cutaneous capillaries or muscles respectively, so that the resistance to the onward movement of blood is lessened, and the left ventricle, thus relieved, is able to complete its systole. At the same time, from the moderate and gentle character of the exercises, compression of the veins, such as occurs in severe muscular exertion, driving on the blood to the right ventricle and causing dyspnea, does not take place. There is thus a transfer of blood from the venous to the arterial system, which is the reverse of the tendency in most forms of heart disease."

Without doubt, the Schott treatment, especially when it is carried out at Nauheim, is frequently followed by excellent results. It is not applicable, however, to every case of heart disease; neither is it entitled to supplant the older and approved methods of treatment. At most, it should be regarded as no more than a valuable auxiliary to rest, diet, and drugs. It must be admitted, too, that home treatment with artificial baths and resistance exercises, while not wholly wanting in efficacy, is much less beneficial than a course of treatment at Nauheim. Change of air and scene, the regulation of the mode of life of the patient, rest, and quiet unquestionably contribute largely to the success which has been achieved at this celebrated German spa.

The treatment is chiefly applicable to cases of *cardiac dilatation in which there is but slight degeneration of the myocardium*. The contraindications are advanced degeneration of the myocardium, pronounced arteriosclerosis, and aneurysm.

COLD

Cold applications may be local or general. Locally, cold may be applied by means of cloths wrung out of iced water, an ice-bag, an ice-poultice, or Leiter's tubes. Heat may also be abstracted by spraying the part with a highly volatile liquid, such as ether or ethyl chlorid. An ice-poultice may be made by sewing up tightly in rubber cloth or a coarse towel crushed ice

mixed with salt and sawdust, bran, or ground flaxseed. Leiter's tubes are flexible metal tubes arranged in the form of coils to fit the head, chest, abdomen, and other parts of the body. Two long rubber tubes are connected with the coil, one to carry ice-water from a reservoir placed a few feet above the patient's head, the other to conduct the water after its passage through the coil to a pail placed on the floor near the bed. Leiter's tubes are especially useful when the cold is to be applied continuously.

Local applications of cold abstract heat from the part, lessen the sensibility of the peripheral nerve-filaments, cause constriction of the bloodvessels traversing the tissues exposed to the cold, and even affect reflexly, as Winternitz has shown, the vascularity of parts remote from the seat of the application.

Cold may be applied to the whole or to a considerable portion of the body in several ways: By cold sponging, the cold pack, the cold douche, or the cold bath.

Cold sponging consists in freely sponging the body with water at a temperature of from 80° to 70° F. (27.5°–21° C.), care being taken not to expose more than one part at a time. The sponging may be made more effective by adding a little alcohol or vinegar to the water.

In applying the *cold pack*, the bedding is first protected by water-proof sheeting; the patient is then stripped and enveloped in an ordinary sheet wrung out of water at a temperature of 70°–60° F. (21°–15.5° C.). The sheet should be well tucked in at the neck and feet, and closely adapted to all parts of the body. The pack is usually continued for from ten to fifteen minutes, and during this time it is necessary to sprinkle the sheet at frequent intervals with water sufficiently cool to maintain a uniform temperature.

The *cold douche* may be given by placing the patient, wrapped in a sheet, in a bath-tub, and then pouring cold water on him from a pail or watering-pot, or the water may be conducted through a rubber tube attached to a faucet and directed to various parts of the body.

In the *cold bath* the temperature of the water may range from 90° to 60° F. (32°–15.5° C.), and the immersion may last from a minute or two to twenty or even thirty minutes, according to effect desired.

When cold is applied suddenly to a considerable portion of the body of a man in good health, the immediate effects are contraction of the cutaneous vessels, pallor of the surface, erection of the papillæ of the skin (*cutis anserina*), momentary catching of the breath, and a feeling of coldness, with shiver-

ing. On coming out of the bath, vigorous subjects, especially if the skin be well rubbed, quickly experience a reaction. The cutaneous vessels dilate, the skin becomes flushed, and the patient feels warm and exhilarated. In delicate subjects, especially if the immersion be somewhat prolonged, this reaction may be very imperfect or altogether wanting, in which case the patient may remain chilly and depressed for several hours after the bath. When followed by a good reaction, cold bathing exerts a powerful tonic effect. It sharpens the appetite, aids digestion, promotes tissue-change, and favors the elimination of waste-products. In pyrexia, general applications of cold lower the temperature, increase the flow of urine, strengthen and slow the pulse, and invigorate the nervous system.

Therapeutics.—In the early stage of *acute inflammation*, especially that resulting from traumatism, a cold-water dressing is often beneficial. In *diphtheria*, *scarlet fever*, and *acute tonsillitis* the application of cold compresses or of an ice-bag to the throat generally affords more relief than poultices or fomentations. In *chilblain* or *frost-bite* the intensity of the reaction may be moderated by rubbing the part with snow or ice. In *lobar pneumonia*, when the temperature is high and the pulse strong, an ice-bag or an ice-poultice adjusted over the affected lung reduces the fever, allays the pain, and quiets the patient. In *acute dysentery* Wood has found ice-suppositories inserted for a length of time, one after another, very useful in allaying tenesmus. An ice-cap or an ice-bag may be applied to the head with advantage in *meningitis*, *apoplexy*, *cerebral congestion*, *headache*, and the *delirium of fevers*. In *neuralgia* dry cold sometimes affords temporary relief, but, as a rule, heat is more grateful. In *exophthalmic goiter*, *paroxysmal tachycardia*, and *symptomatic palpitation* an ice-bag or a Leiter's coil over the precordium often exerts a sedative influence upon the heart. An ice-bag may also temporarily relieve distress in *aortic aneurysm*, especially when the sac is superficial. Prior to the performance of acupuncture or of paracentesis or to using the actual cautery, *local anesthesia* may be secured by spraying the part with ethyl chlorid or ether, or holding over it for a few minutes a block of ice which has been sprinkled with common salt. In *internal hemorrhage* the application of an ice-bag over the affected region is a useful adjuvant to other measures.

General applications of cold are used for their antipyretic and tonic effects. In *typhoid fever* and other *continued fevers* hydrotherapy gives excellent results. There is ample evidence to show that the mortality of typhoid fever in general hospitals may be considerably reduced by the bath treatment advocated by

Brand, of Stettin. The details of this treatment are as follows: A bath-tub half full of water at 70° F. (21° C.) is kept in readiness near the bed, and every third hour, if his temperature is above 102.2° F. (39° C.), the patient is wrapped in a sheet and carefully lifted into the water. While in the bath an ice-cap is kept upon the head or cold affusions are applied to it, and the trunk and limbs are vigorously rubbed, so as to bring new relays of blood to the surface. A stimulant is sometimes given before the bath to lessen the shock. At the end of fifteen or twenty minutes the patient is carried back to bed and covered with a dry sheet and a light blanket. After he has been thoroughly dried, the damp coverings are removed and replaced by dry ones. If the patient be delicate, it is preferable to place him in a bath of 90° F. (32° C.), and then gradually lower the temperature of the water to 70° F. (21° C.). The good effects of the bath are: Reduction of temperature, increased secretion of urine, marked improvement in the pulse, and lessening of the nervous symptoms—delirium, stupor, insomnia, and subsultus tendinum. The only contraindications are perforation, hemorrhage, menstruation, and persistent prostration after the bath. Shivering and blueness naturally follow the bath, and, unless very prolonged, are not to be considered contraindications.

When the baths are not well borne, or the temperature shows no tendency to exceed 102.2° F. (39° C.), cold sponging or the cold pack may be substituted for immersion.

The *hyperpyrexia of thermic fever*, or of *acute rheumatism* should be treated by immersing the patient in water containing crushed ice, or, better, by rubbing him with blocks of ice for ten or fifteen minutes.

In *neurasthenia* and *hysteria* hydrotherapy in the form of the cold spray, cold douche, or cold bath, is often a valuable auxiliary to rest, massage, and isolation. It is very important, however, not to institute the treatment too abruptly, as otherwise it may prove harmful rather than beneficial. In *chorea of childhood* the wet-pack (80°–70° F.—26.5°–21.0° C.) is sometimes very beneficial.

HEAT

Heat may be applied in the dry or moist form, and the application may be local or general. Locally, dry heat is applied by means of hot cloths, bran-bags, water-bags or water-bottles, or local baths of superheated dry air. Moist heat may be applied by means of fomentations, poultices, or the douche. Hot-water baths are also applicable to certain limited portions

of the surface of the body. Heat, locally applied, allays irritation of the peripheral sensory nerves, dilates the cutaneous vessels, increases the secretion of sweat, and probably, like cold and counterirritation, exerts reflexly some influence on the nutrition of the superficial tissues, and even of the underlying organs. Intense dry heat (250° F.—121° C.) not only affects the tissues to which it is directly applied, but also produces general diaphoresis, raises the body-temperature two or three degrees, and increases the frequency of the pulse.

Dry heat may be applied to a considerable portion of the body by means of the hot-air bath. This is best given with the patient in bed, heat being conducted under the bed-clothes through an inverted funnel and L-shaped metal tube from a spirit lamp resting upon the floor, or generated by 6 or 8 incandescent electric light bulbs attached to a board which is suspended from the frame of the canopy. The patient is stripped and wrapped snugly in a blanket, and the bed-clothes, over which have been spread a rubber sheet and an extra blanket, are slightly raised by means of a cradle, so that the hot air can freely enter and surround the body. The bath may last from 15 to 30 minutes. The effect of a general application of dry heat may also be obtained in the Turkish bath. In this the patient is conducted through a series of heated apartments, the first having a temperature of 100° F. (38° C.) and the last 150° F. (66° C.) or above. After perspiration has been freely established, he is thoroughly shampooed and rubbed, and then given a cold douche or a plunge-bath.

A modified form of Turkish bath may be given in a portable electric-light cabinet. This is so arranged that the entire body, with the exception of the head, is subjected to the heat given off by 20 to 60 incandescent lamps. The temperature in the cabinet ranges from 120° F. (49° C.) to 177° F. (80° C.) according to the number of lamps, the amount of air that enters from the outside, and the type of thermometer that is used. A thermometer with a blackened bulb registering considerably higher than one with a bulb of clear glass. During the bath the head should be kept cool by cloths wrung out of cold water, and after the bath the body should be rubbed with tepid water and then with alcohol and water. The skin should be dried by mopping rather than by rubbing, as the latter by dilating the cutaneous vessels tends to maintain the sweating. The patient should cool off gradually and should remain indoors for at least 2 hours.

The general application of moist heat may be obtained by means of the hot-water bath, hot-pack, or hot vapor-bath. In the hot-water bath the temperature of the water should be at

first about 98° F. (37° C.), but this should be raised gradually while the patient is still in the bath to 105° F. (40.5° C.) or even to 110° F. (44° C.). The bath may last, according to circumstances, from 15 minutes to half an hour or longer. In the warm bath the temperature may range between 98° and 85° F. (37°–30° C.).

The hot-pack is given by closely enveloping the patient in a blanket wrung out of hot water, covering him with two or more blankets and a rubber sheet, and then placing hot bottles at each side and at his feet. The pack may last from half an hour to an hour. A hot vapor-bath may be given in the same way as a hot-air bath, steam from a boiling kettle being conducted under the bed-clothes instead of hot dry air, or the steam may be generated under the bed-clothes by placing about the patient hot bricks or plates which have been wrapped in wet cloths. In the Russian bath, also, steam replaces the hot dry air of the Turkish bath.

The first effects of the general application of heat are dilatation of the cutaneous vessels and the establishment of free perspiration. The administration of cool drinks during the exposure makes the application more effective by driving the blood from the interior to the surface of the body. There is, ordinarily, no marked rise in the central temperature of the body, since the accumulation of heat is prevented by the free sweating. If, for any reason, diaphoresis does not occur, however, the central temperature may rise somewhat—even to a dangerous point if the exposure be prolonged. The chief secondary effect of the general application of heat is increased elimination of effete matters from the body. Dry heat is generally more effective than moist heat, since it induces more copious perspiration.

In sudden failure of the circulation, such as occurs in shock and collapse, the general application of heat not only serves to raise the body-temperature, but also acts as a powerful cardiac and vasomotor stimulant. On the other hand hot baths increase metabolism and if too hot, too prolonged, or used too frequently may cause dangerous depression, especially in persons who are already debilitated.

Therapeutics.—Heat, both dry and moist, makes a valuable local application in a large number of *acute inflammatory diseases*. Generally, it may be used interchangeably with cold, the chief guide in the selection of one or the other being the feeling of the patient. Moist heat in the form of fomentations or hot baths is a valuable adjuvant to morphin in relaxing the spasm of unstriated muscles which occurs in *intestinal, biliary,*

and *nephritic colics*, in *spasmodic croup*, and in *retention of urine*. Hot baths are also useful in breaking up *general convulsions*, especially those occurring in children. Hot foot-baths, through their reflex effect upon the circulation, often afford relief in *cerebral congestion*, *acute coryza*, and *amenorrhea from exposure to cold*. In *acute and chronic parenchymatous nephritis* hot-air baths, hot-packs, and hot-water baths are often of great service in producing diaphoresis, especially when there is dropsy or uremia. Mention has already been made (p. 530) of the efficacy of warm effervescent baths in certain cases of *chronic heart disease*. The continuous immersion of the patient in a warm bath (90°–100° F.—32°–38° C.) has been found useful in *extensive burns* and in some cases of *phagedena*. A course of Turkish baths is frequently beneficial in *chronic gout* and in the earlier stages of *chronic nephritis*.

In acute conditions attended with subnormal temperature, such as *surgical shock* and *collapse from disease or poisoning*, the general application of heat, especially in the form of the warm bath, is an important factor of the treatment.

The local application of intense dry heat (200°–250° F.—93°–121° C.) by means of some such apparatus as was invented by Tallerman, in 1893, is often advantageous in certain affections of the joints, especially in *chronic synovitis*, *traumatic arthritis*, *subacute and chronic infective arthritis*, *sprains*, *tendinous inflammations*, and in the after-treatment of *fractures and luxations*.

HYPODERMOCLYSIS AND INFUSION

Hypodermoclysis and infusion are the introduction, into the subcutaneous tissues and bloodvessels, respectively, of weak saline solutions in considerable quantities. These procedures, first brought prominently forward by Cantani during the cholera epidemic of 1892, have been found of great value in a number of conditions. They serve to restore vascular fulness when, from any cause, the volume of blood has been much reduced, to stimulate the heart, especially when cardiac failure is associated with arterial depletion, to dilute any toxic substances that may be present in the blood, and to eliminate toxic substances by promoting diuresis.

In *hemorrhage* the injection of a saline solution affords a potent means of rapidly restoring the volume of blood. It is much more easily practised than transfusion of blood, although the latter is more effective.

Hypodermoclysis or infusion has proved very beneficial in many severe *toxemic conditions*; thus, it has been found effica-

cious in *uremia*, *diabetic coma*, *puerperal eclampsia*, and *septicemia*. It has given good results also in *cholera*, *thermic fever*, and extensive *burns*. In *uremia*, *eclampsia*, and *thermic fever* it is often more effective if preceded by venesection. Lastly, it is exceedingly useful in combating the low bloodpressure of *shock*. The solution usually employed for these injections is a decinormal salt solution (0.6 per cent.). This solution is selected because it corresponds closely in saline strength to the blood-serum. It may be prepared by adding a heaping teaspoonful of salt to a quart or a liter of water, boiling, and filtering. Plain water cannot be used on account of its solvent action on the blood-corpuscles. Various other formulæ, some quite complicated, have been suggested, but the majority of them have no advantages over normal saline solution. However, in some cases of *shock* or of *exhaustion* resulting from severe infections lack of nourishment, persistent vomiting, or a great loss of the body fluids a solution of glucose is useful. For subcutaneous injection a 5 per cent. solution and for intravenous injection a 5 to 10 per cent. solution may be employed. As much as 1000 mls of the weaker solution may be given in 24 hours. The glucose may be given alone in water or dissolved with salt. The solution should be filtered and sterilized, a 5 per cent. solution of sodium bicarbonate with salt, given intravenously, to the extent of 500 mls or more, is apparently of some value in *shock*, *diabetic coma*, and other conditions in which the alkali reserve of the body is much reduced. Subcutaneous injections of alkaline solutions should be avoided as not rarely they cause sloughing.

Owing to the rapidity with which normal salt solution escapes through the capillary walls into the tissue spaces in such conditions as traumatic shock and post-hemorrhagic anemia, the addition of a colloid, 6 or 7 per cent. of gum acacia, to the salt, has been advocated (Bayliss). This "gum-salt" solution has the same osmotic pressure and viscosity as blood plasma, does not agglutinate the corpuscles, does not readily escape through the capillaries, and is not affected by sterilizing heat. However, chills may follow the infusion and occasionally there is serious collapse.

When the circulation is fairly active and there is no great emergency, hypodermoclysis should be practised in preference to infusion, the injection being made in the cellular tissue of the ilio-lumbar region, chest, abdomen, or thigh. The fluid may be introduced by means of a fountain syringe to the tube of which has been attached an aspirating needle of moderate size. The apparatus, the hands of the operator, and the region selected for the puncture should be thoroughly sterilized. The bag should be suspended 2 or 3 feet above the patient, and the solution

should flow from the needle while the puncture is being made. The fluid should enter the tissues at a temperature of about 105° F. (40° C.), and to insure this a temperature of 110° F. (44° C.) should be maintained in the bag. The quantity of fluid required varies from 8 ounces (250.0 mls) to a pint (0.5 L.) in toxemic conditions, and from a pint (0.5 L.) to a quart (1.0 L.) or more in severe hemorrhage or shock. Frequently, better results are obtained by injecting smaller quantities several times than a larger quantity at once. In children from 2 to 4 ounces (60.0–120.0 mls) are usually sufficient. The rapidity of absorption varies with the state of the circulation, from twenty minutes to an hour being required to introduce a pint of fluid. To prevent overdilatation of the tissues, the fluid should be made to enter slowly, gentle friction being applied to aid absorption.

In cases of emergency, when the circulation is very feeble and absorption is nearly at a standstill, intravenous infusion affords a more rapid means of filling the vessels and stimulating the heart than hypodermoclysis. For infusion the apparatus may consist of a graduated glass irrigating jar, having a capacity of about 2 quarts (2.0 L.), and provided with rubber tubing. To the latter should be fitted a fine transfusion cannula having a blunt, oblique tip. In great emergency a glass funnel, a rubber tube, and an aspirating needle will suffice. The reservoir should be placed about 2 feet above the patient, and its contents should be constantly maintained at a temperature of about 110° F. (44° C.), or higher (115° F.—46° C.) in cases of profound shock. The operation is performed as follows: The arm is prepared as for venesection, a fillet being applied securely some distance above the elbow. A prominent vein, preferably the median basilic or the basilic, is then exposed by dissection, and a ligature tied around it at the distal end of the wound. A second ligature is placed around the vessel at the proximal end of the wound, but it is not tied. The vein is next incised between the ligatures, and the cannula, while fluid is escaping from it, is carefully inserted into the lumen of the vein and tied in place by the second ligature, after which the fillet is *immediately* removed. From ½ pint to 2 pints or more (250.0–1000.0 mls) may be infused, according to the condition of the patient. The rate of flow may be regulated by raising or lowering the reservoir or by means of a clamp attached to the tubing. At least ten minutes should be allowed for introducing each pint of fluid. If care be taken to expel all air from the tubing and cannula before inserting the latter, the danger of air-embolism need not be feared.

Shortly after infusion a rigor may occur, and the pulse and respiration may become more rapid; usually, however, these

untoward symptoms gradually disappear and are followed by distinct improvement.

ENTEROCLYSIS

By enteroclysis is meant the irrigation of the colon with large quantities of water, the latter being either plain or medicated, hot or cold, according to the effect desired. It is practised for a number of purposes: To cleanse the colon; to bring remedies in direct contact with the lower bowel in diseased conditions; to raise or lower the body-temperature; to stimulate the heart in shock or collapse; to restore water to the blood in anhydremia; to promote renal secretion; and to dilute poisonous substances that may be present in the blood.

In some cases of *intestinal stasis* good results may be obtained by thoroughly irrigating the lower bowel at intervals of two or three days with several quarts of water at from 90° to 70° F. (32°–21° C.).

In *acute catarrhal colitis* injections of warm (103° F.—39.5° C.) normal saline solution or of a boric acid solution (1 dram to 1 quart—4.0 gm. to 1.0 L.), continued until the fluid returns from the bowel clear, often affords much relief.

In *amebic dysentery* a solution of quinin (1:5000 to 1:2000) or of silver nitrate (see p. 369) may sometimes be used with advantage.

In *ileocolitis* and *cholera infantum* enteroclysis, once or twice a day, with normal salt solution is a valuable adjuvant to other therapeutic measures. If the child's temperature is high the water may be at 90° F. (32° C.) or lower; if, however, there is a tendency to collapse, the water may be at 105° F. (40° C.). Cantani and others have had good results from enteroclysis with hot tannin solutions (2 per cent.) as an aid to hypodermoclysis in *Asiatic cholera*. Hot saline injections are frequently efficacious in *anuria* resulting from nephritis or following operations. In *uremia* they tend not only to promote renal secretion, but also to dilute the toxic substances circulating in the blood. Rectal infusions of hot saline solution (110° F.—43.5° C.) are helpful in the milder forms of *shock* and *hemorrhage* and in the more severe cases are a valuable adjuvant to intravenous infusion or hypodermoclysis.

Daily irrigation of the bowel with cold water—70° F. (21° C.) or lower—is sometimes of service in *chronic catarrhal jaundice*, in *internal hemorrhoids*, and in *inflammatory conditions of the rectum prostate, deep urethra, etc.* Both very cold (50° F.—10° C.) and very hot (115° F.—46° C.) irrigations have been recom-

mended in *hemorrhage from the bowel*. Enemas of cold water (60°–50° F.—15.5°–10° C.) may also be used advantageously in conjunction with cold baths to lower the temperature in *thermic fever*.

Continuous proctolysis, or the instillation of saline solution into the rectum at a very low pressure or drop by drop, as originally employed by Murphy, affords an excellent means of restoring fluid to the vessels and tissues, stimulating the heart, and promoting the elimination of noxious materials. It has been found especially useful in *acute peritonitis*, *septic conditions*, *uremia*, and *mild forms of shock*. It is also an excellent means of relieving *thirst* after abdominal operations. A solution containing sodium bicarbonate (5 per cent.) and glucose (5 per cent.) with salt is sometimes preferred to the simple saline solution. In grave conditions from 2000 to 3000 mils of the fluid may be given each 24 hours.

Enteroclysis may be practised by means of an ordinary fountain syringe to which has been adjusted a flexible colon tube, or, for children, a soft-rubber catheter (No. 20). If the latter be used, an extra eye should be cut in it near the tip. The requisite pressure is secured by elevating the water-bag 3 or 4 feet above the patient. The return flow may be collected in a bed-pan or, better, it may be conducted, by the aid of a rubber sheet, into a bucket placed on the floor. The patient having been placed in the dorsal position with the hips elevated, the tube should be well lubricated and gently inserted first upward and forward for a distance of two or three inches and then upward and slightly backward. For high irrigation, the introduction of the tube is facilitated by allowing the solution to flow gently as soon as the anus is passed. While a long single tube gives good results, a double-current tube such as that devised by Kemp, Tuttle or Bodenhamer, is much more convenient, especially for continuous irrigation.

LAVAGE OF THE STOMACH

There are two methods of washing out the stomach—one, by the stomach-pump, the other, by siphonage. The stomach-pump is simply a syringe with two apertures instead of one, in which are adjusted valves opening in opposite directions. By connecting the syringe alternately at each of these apertures with an incompressible tube passed into the stomach, the gastric contents may be drawn out or fluid may be introduced into the stomach. The siphoning apparatus, on account of its simplicity and safety and the ease with which it can be manipulated, even

by the patient himself, has almost completely supplanted the stomach-pump. The latter may be used with advantage, however, when the stomach contains much coarse solid matter or when it is necessary to remove the gastric contents very promptly and thoroughly.

The siphoning apparatus consists of a soft-rubber stomach-tube, joined through the medium of a short piece of glass tubing to a piece of rubber tubing about 3 feet long (90 cm.), to the free end of which is fitted a large glass funnel. The stomach tube should be about $2\frac{1}{2}$ feet (75 cm.) long and from $\frac{1}{4}$ to $\frac{1}{2}$ inch (6 to 12 mm.) in diameter. During the operation the patient should be in a sitting or semiupright position with the head inclined slightly forward. No other lubricant than water is required for the stomach-tube. The introduction of the tube is facilitated by having the patient breathe deeply and make repeated efforts at swallowing as soon as the pharynx is reached. Cocainization is sometimes employed to allay extreme sensitiveness of the pharynx, but it is rarely necessary. The requisite amount of water, usually a pint (500 mls), is poured into the funnel, which is then elevated sufficiently to allow the water to flow into the stomach. Before the funnel is empty, however, it is quickly depressed, so that the water is returned from the stomach by siphonage. The escape of the fluid from the stomach may be facilitated by the application of gentle pressure over the epigastrium. The process should be repeated until the water returns clear.

For an infant a soft rubber catheter (24 French) may be used as a stomach tube and this may be passed through a nostril.

Ordinarily, the water used for lavage may be unmedicated; when, however, there is abundant mucus in the stomach, 2 per cent. of sodium bicarbonate may be added with advantage. Potassium permanganate (1:5000), sodium salicylate (1:100), or sodium hyposulphite (1:100) may be used when there is excessive fermentation.

The most important indication for lavage is *retention of food with fermentation*. Thus, in organic stenosis of the pylorus thorough washing of the stomach two or three times weekly, or every day in some cases, preferably before breakfast, or 3 or 4 hours after supper, affords great relief. In *atonic dilatation with fermentation* lavage is also efficacious. In *acute food-poisoning* and *toxic gastritis* it is often better to resort to the tube than to employ an emetic.

In *chronic gastric catarrh*, if there is an *excessive secretion of mucus*, lavage may be of service; in other cases, however, it does no good, and is, according to Boas, absolutely contraindicated.

Practised promiscuously in cases of simple gastric catarrh, it is capable of doing considerable harm and of developing into a most pernicious habit. In *supersecretion of acid* (Reichmann's disease) washing out the stomach with a solution of sodium bicarbonate (2 per cent.) or silver nitrate (1:5000 to 1:2000) sometimes gives good results. Kussmaul and others have found lavage of the stomach very beneficial in *acute intestinal obstruction*. In this condition it serves to allay vomiting, to lessen the pressure in the bowel, and to diminish the violent peristalsis.

Lavage is contraindicated in peptic ulcer, in ulcerating carcinoma, especially when accompanied by much bleeding, and in gastric catarrh associated with atrophic cirrhosis of the liver. It should be avoided also in advanced pregnancy, in aortic aneurysm, in pronounced cardiac decompensation, and in aged persons with marked arteriosclerosis.

BLOODLETTING

Bloodletting is employed both as a local and as a general remedial measure. As a local measure it may be practised by cupping or by leeching, and as a general measure by venesection.

Cupping.—There are two methods of cupping—the dry and the wet. In dry cupping the blood is not shed, but is diverted by atmospheric pressure from the deeper parts to the cutaneous surface. A small quantity, however, is actually drawn from the vessels into the cellular tissue of the skin. The special instrument used for cupping consists of a glass bell with an aperture at its summit, through which is extracted the air by means of a pump or rubber ball. In the absence of such an instrument, an ordinary tumbler will serve the purpose. A small piece of blotting-paper moistened with alcohol is fastened in the bottom of the tumbler and lighted. While the paper is still burning the glass is inverted and applied firmly to the skin which has been moistened with warm water. The flame is almost immediately extinguished, and the air being exhausted, the skin in the interior rises in the cup and becomes of a dark-red color. To avoid burning the skin, it is necessary to allow all excess of alcohol to run out of the tumbler before igniting the paper. From six to a dozen of these cups may be applied, and they may be allowed to remain in position for from five to ten minutes. The cup can be readily removed by making a little pressure near the rim, so as to allow air to enter. The same method is pursued in wet cupping, except that a number of small incisions are first made in the skin, preferably after it

has become congested by dry cupping. The incisions, which may be made with a scalpel or a special scarificator, should involve the skin only, otherwise the fat of the subcutaneous is likely to be drawn into them when the vacuum is produced as scarification leaves permanent cicatrices, wet cups should not be applied upon exposed surfaces. Dry cupping is less effective, as a rule, than wet cupping, but it is easily practised.

Leeching.—Leeches accomplish the same purpose as wet cups, but on account of their size and shape they can be applied to parts to which cups cannot be adjusted, as behind the ears, about joints, over the spermatic cord, and the verge of the anus. Each leech, according to the variety employed, removes from 1 to 4 drams (4.0–15.0 mls) of blood. Leeches should be applied in the neighborhood of inflamed parts, not directly over them, and parts which are abundantly supplied with loose areolar tissue, such as the eyelids and the scrotum, should be avoided. The eye may be depleted from the temple, and the testicle from the perineum. Before leeching, the part should be shaved and well washed, care being taken to remove all soap.

Leeches may be applied with the finger or by means of an inverted wine-glass or pill-box. A little blood or warm milk smeared over the skin will generally induce them to bite, if they are not disposed to do so. They should not be detached forcibly, but allowed to drop off themselves, or made to relinquish their hold by sprinkling them with salt. If desirable, bleeding from the bites may be encouraged by applying warm fomentations. Occasionally, owing to the presence in the tissues of a large quantity of the anti-coagulant substance secreted by the leech, the hemorrhage proves very persistent, and requires for its arrest the application of firm pressure, of some styptic (ferric subsulphate or alum), or of the actual cautery. Like scarifying, leeching leaves indelible scars.

Local bloodletting may often be practised with advantage in the early stage of many acute inflammatory diseases, such as *pneumonia*, *nephritis*, *orchitis*, etc. At the onset of acute inflammation of serous membranes—*pleuritis*, *pericarditis*, *iritis*, *synovitis*, and *meningitis*—especially when the symptoms develop abruptly and are very severe, it may be of the greatest value in relieving pain and in repressing exudation. In *acute pulmonary edema with cyanosis* wet cupping is of service, although it is not generally so useful as venesection.

Venesection or Phlebotomy.—The general abstraction of blood is accomplished by incising a vein. The patient having been placed in a semirecumbent position, the arm should

be constricted a few inches above the elbow by a twisted handkerchief or a few turns of a roller bandage. If this is not sufficient to render the veins prominent, the arm may be rubbed for a few minutes from below upward. A large vein (median cephalic or median basilic) having been selected, it should be fixed by the thumb of the left hand below the point of section, and then incised by a lancet or bistoury in a direction oblique to the long axis of the vessel. The pulse should be carefully observed during the operation, and when it lessens in force or becomes more compressible, the bleeding must be suspended. The loss of blood required to afford relief varies in different conditions from a few ounces to a pint or more. To arrest the flow, it is only necessary to remove the fillet from the arm and to apply a small compress and figure-of-eight bandage.

The cases in which venesection is indicated are those in which life is immediately endangered by acute circulatory embarrassment or by toxemia. In *overdistention of the right ventricle*, whether from mitral disease, pneumonia, or emphysema, when there is a small, weak pulse, with cyanosis and orthopnea, the venous engorgement is often promptly and effectually relieved by the abstraction of from 10 to 15 ounces (300–450 mls) of blood. In *cerebral hemorrhage*, if the pulse tension is high and there are evidences of pronounced hyperemia of the brain, venesection is advisable. In *aortic aneurysm*, if the heart-action is strong and there is severe pain, bleeding often affords relief.

In *acute uremia* and *puerperal eclampsia* venesection affords the most rapid means available of removing toxic substances from the body. It may be practised advantageously in connection with subcutaneous and rectal injections of normal salt solution.

Packard and others have found bloodletting (300–450 mls) efficacious in *grave cases of thermic fever*. Feebleness of the pulse is not necessarily a contraindication, as the circulation often improves as the blood flows from the arm.

TREATMENT BY HYPEREMIA

Treatment by hyperemia is based upon the theory that an increased amount of blood in an inflamed part is useful in antagonizing bacterial growth, in preventing the spread of the disease process, in promoting absorption and in favoring resolution. Two forms of hyperemia are employed, namely, active or arterial and passive or venous.

Active hyperemia may be produced by irritant drugs, such as oil of turpentine or mustard, by heat obtained from hot-water bags,

hot compresses, hot poultices, electric pads, etc. or by hot air in a dry form. It is of definite value in *neuralgia*, *myalgia*, and various deeply seated *inflammatory conditions*. A very high degree of dry heat (150°–250° F.) for local use may be obtained by means of one of the many hot-air boxes or so-called baking apparatuses on the market. These are made to fit various parts of the body, such as the foot, knee, hand, arm, shoulder, etc. and are provided with cuffs of felt and pads of asbestos to prevent contact with the metal. The danger of burning is averted by the rapid evaporation of the free perspiration, which is made possible by holes in the box for ventilation. The heat may be applied for half an hour or an hour daily or several times a week. This method of treatment often acts very favorably in *chronic synovitis* and in *chronic infective* and *traumatic arthritis*. It is especially effective in conjunction with gentle massage. It should be avoided in tuberculous and gouty arthritis.

Passive hyperemia, the value of which has been especially emphasized by Bier, may be produced by the use of elastic bandages which obstruct the venous circulation or by various forms of vacuum cups. The method of producing hyperemia by constricting bands is best adapted for the foot, hand, elbow, and knee; the shoulder is less favorable for it, and it cannot be applied to the hip joint at all. Lesions in the testicle and epididymis are amenable to this treatment. An ordinary Esmarch bandage or, in the case of the shoulder or testicle, rubber tubing may be used for the purpose. The constriction should be made some distance above the seat of the inflammation and should be sufficient to slow the venous return without interfering with the arterial supply. When the elastic band is properly applied, the part distal to the point of constriction acquires a reddish blue color and becomes warm to the touch, and the pain is relieved rather than intensified. Pallor or a bluish gray hue, coldness, or pain indicates that too great a degree of compression is being used and that the blood is being kept out of the part instead of being forced into it. Bier's hyperemic treatment by elastic bands has been found beneficial in *acute and chronic pyogenic infections of the joints*, *gonorrheal arthritis*, *tuberculosis of the bones*, *joints and testicles*, *felons*, *leg ulcers unaccompanied by varicose veins*, etc. Except in tuberculous processes, the applications may be made for two periods of from 8 to 10 hours out of each twenty-four hours. In tuberculous conditions short applications of from one to three hours a day over a period of months are advisable. In chronic cases it may be necessary to place the part for ten or fifteen minutes in a bath of hot water before making the constriction. Open wounds should be covered with moist antiseptic gauze before the hyperemia is induced.

Hyperemia by means of vacuum cups often gives good results in *acute mastitis, furuncle, carbuncle, abscess, bubo, etc.* Cups of all sizes and shapes have been devised, the vacuum being produced by a rubber bulb or a special pump. The cup should be large enough to rest everywhere on sound tissue and the suction should be sufficient to produce a bluish-red tint. The occurrence of a dark blue color, the aspiration of blood, or complaint of pain is an indication that the degree of suction is too great. If pus is present drainage should always be secured by means of an incision or puncture before the cup is applied. The treatment should be practised for five minutes, with free intervals of two or three minutes, over a period of from one-half to one hour each day. At the end of the treatment, the part should be bathed and the loose or necrotic tissue removed by sterile gauze or forceps, and then a simple wet dressing should be applied.

Hyperemic treatment requires considerable skill and patience and unless properly carried out is likely to do much more harm than good. Even with correct technique, unsatisfactory or unfavorable results are the rule in erysipelatous processes, in lesions accompanied by venous thrombosis, and in diabetic furuncles or carbuncles.

SPINAL PUNCTURE

The procedure known as spinal or lumbar puncture consists in the removal of cerebrospinal fluid through a hollow needle introduced between the transverse processes of the lumbar vertebræ. Since 1891, when it was first resorted to by Quinke, for the relief of excessive intracranial pressure in cases of chronic hydrocephalus, it has been extensively practised not only as a therapeutic measure, but also for diagnostic purposes. The puncture is made usually between the third and fourth lumbar vertebræ, the needle, which should be of nickel or platinum and at least $3\frac{1}{2}$ inches (9 cm.) long, being introduced from 5 to 10 mm. to one side of the median line and directed slightly upward and inward. A line drawn between the highest points of the iliac crests with the patient erect passes through the tip of the fourth lumbar vertebra. The patient may sit in a chair with the body bent well forward or he may lie on his left side with his knees drawn up and his body arched forward. The part should be sterilized with iodine and anesthetized with procaine or by freezing, and the skin should be incised with a scalpel. The required depth of the puncture can be determined by the sense of touch, the disappearance of resistance indicating the entrance of the needle into the spinal canal. In adults the fluid is usually reached at a depth of

from $2\frac{1}{2}$ to 3 inches (6 to 7.5 cm.), and in children at from 1 to $1\frac{1}{2}$ inches (3 to 4 cm.). From 10 to 50 mils or more of fluid may be withdrawn, the amount depending upon the age of the patient and the strength of the flow through the needle. Upon the occurrence of pallor, faintness, dizziness or headache the needle should be withdrawn. Under no circumstances should the fluid be aspirated. The operation is completed by sealing the puncture with cotton and collodion, and after its completion it is advisable for the patient to remain in bed for twenty-four hours.

As a therapeutic measure, spinal puncture is employed to relieve excessive pressure by the cerebrospinal fluid on the brain and cord; to remove pus and toxic products from the cerebrospinal fluid; as a means of administering antitoxic sera in meningococcus meningitis and tetanus and arsphenamin or neoarsphenamin in syphilitic diseases of the central nervous system; and for the purpose of producing spinal anesthesia.

In *meningococcus meningitis* the operation is not only of service in administering antimeningococcus serum, but when frequently repeated is of considerable value in itself, as it affords a means of draining the infected canal. In *tuberculous meningitis* lumbar puncture may be employed as a palliative measure when the pressure symptoms are severe. In *chronic serous meningitis* it may prove curative. *Chronic hydrocephalus* is not often benefited by the withdrawal of fluid from the spinal canal, but the operation may afford temporary relief if the obstruction to the ventricular outlet is incomplete and the fluid is produced in excess. Drainage by lumbar puncture is sometimes efficacious in *acute uremia* and in *delirium tremens*. The procedure is dangerous in the case of intracranial tumors or similar processes, especially if these are in the posterior cranial fossa, as with decompression the medulla is likely to be jammed down into the foramen magnum. Because of its effect upon the intracranial and intraspinal pressure, it may also prove disastrous in case of hemorrhage. Schönbeck in 1915 collected reports of 70 deaths from lumbar puncture, and this number is probably but a small proportion of those that have actually occurred. In 37 cases there were intracranial tumors and in 13 hemorrhage.

ROENTGEN RAY TREATMENT

While experience has shown that many of the claims originally made for it were not justified, roentgen ray treatment is conceded to be a valuable addition to our resources and in certain diseases to be more efficacious than any other measure. X-rays differ

from actinic rays in having greater penetrating power, in being only feebly bactericidal, and in being capable of effecting curative changes without producing any pronounced inflammatory reaction. The nature of the changes produced by roentgen rays in animal tissues is somewhat obscure. It seems to have been demonstrated, however, that mild applications exert a stimulating and strong applications a destructive effect, the sensitiveness of a tissue to the rays varying with the type of its component cells. Pathologically altered cells are apparently much less resistant to the rays than healthy cells and are devitalized with smaller doses. Whatever the effect, it is produced only after a period of latency.

The first disturbance excited in the *skin* by x-ray action is an erythema resembling sunburn. This usually disappears in a few days or weeks, but with a continuance of exposures, it is succeeded by slight pigmentation and sometimes by exfoliation, a temporary loss of the hair and more or less persistent atrophic changes in both the skin and nails. Occasionally, painful ulceration eventually ensues or keratoses supervene and develop into carcinoma. The application of x-rays to any considerable portion of the body, especially if the hematopoietic organs are exposed, has a pronounced effect upon *metabolism*, regularly causing an increase in the destructive metamorphosis of the body proteins. In patients with leukemia or with unresolved pneumonia the nitrogen excretion may be doubled. Severe constitutional symptoms (malaise, nausea, epigastric and lumbar pain, etc.) sometimes result from the accumulation of the waste products in the system, especially when nephritis exists and elimination is impeded.

Experiments reported by Heinicke and by Krause and Ziegler show that prolonged exposures to x-rays are followed by destructive changes in the *marrow of the long bones*, the *spleen* and the *lymph nodes*. Eventually, the Malpighian corpuscles of the spleen almost entirely disappear and are replaced by connective tissue. The changes in the hematopoietic organs, as those elsewhere, are cumulative, and occasionally an incurable aplastic anemia develops in operators who are not adequately protected from x-ray activity. Even mild exposures to the pelvic region, if frequently repeated, have a pronounced effect upon the *testicle* and *ovary*, producing necrostermia or azoöstermia in the male and an arrest of menstruation and of ovulation in the female. These effects, which may be permanent, are upon the epithelial structures of the gonads and not upon the interstitial glandular tissue, which is concerned in the maintenance of the sexual instinct and activity.

The most important therapeutic application of x-radiation is in the treatment of *carcinoma*. The best results are obtained in the non-metastasizing epitheliomas of the skin, which are, as a rule, readily destroyed. In carcinoma of the buccal mucous membrane roentgen or radium radiation must usually be supplemented by adequate surgical excision. Only in carcinomas of the larynx located above the vocal cords has roentgen irradiation accomplished favorable results. In carcinoma of the cervix of the uterus roentgen therapy from a Coolidge tube, alone or in conjunction with radium applications, frequently results in a local cure, although if metastases have already occurred in the pelvic lymphatics the treatment is only palliative. While there is some difference of opinion as to whether radiotherapy or surgical treatment should be given the preference in carcinoma of the uterine cervix, the majority of clinicians favor excision and advise the restriction of radiotherapy to inoperable and recurrent cases. It is generally agreed that carcinoma of the body of the uterus is best treated by excision. In cases of deep-seated carcinoma, as of the breast, stomach, or intestines, not much can be accomplished by x-ray therapy. In carcinoma of the breast, however, it is sometimes a useful postoperative measure, and in inoperable or recurrent cases it may afford temporary relief and prolong life. *Sarcoma* is, generally speaking, less amenable to radium or roentgen radiation than carcinoma, although lymphosarcoma is sometimes favorably affected by it.

In gynecologic practice roentgen or radium radiation has proved of great value in the treatment of *uterine fibroids* and certain forms of *uterine hemorrhage*. In uterine fibroids it is preferred to surgical operation by many clinicians when the tumor is interstitial, is not very large, is not undergoing secondary changes, and is not accompanied by salpingitis. Cervical fibroids and large pedunculated fibroids are unsuited for radiotherapy.

Hypertrophy of the thymus gland, *chronic tuberculous adenitis*, *mycosis fungoides*, *hypertrichosis* and *leukoplakia buccalis* have each been successfully treated by x-rays. Good results from their use have also been obtained in *favus*, *ringworm of the scalp*, *acne*, *sycosis*, *lupus vulgaris*, *pruritus ani* and *vulvæ* and *alopecia areata*.

The roentgen ray is the most effective means of treating *leukemia*, its application frequently resulting in a reduction of the number of leucocytes to the normal, the disappearance of the splenic tumor and glandular swellings and a great improvement in the patient's general health. The benefit is, however, never permanent and requires frequently repeated applications over a period of several months. Pancoast's method of exposing the

long bones rather than the spleen yields the best results. Lymphoid leukemia is more refractory to x-ray treatment than the myelogenous type, and acute leukemia of either type is likely to be adversely affected by radiotherapy in any form. Roentgenization is also of benefit in *Hodgkin's disease*.

Exophthalmic goiter is often favorably influenced by x-ray therapy, although partial thyroidectomy is usually a more effective measure. X-ray exposures of the long bones and spleen have given encouraging but somewhat indecisive results in *erythremia* or *primary splenomegalic polycythemia*. Anders, Daland and Pfahler report benefit from x-ray applications in *arthritis deformans*, and L'Hermitte, Delherm, Grameque and others report encouraging results from x-radiation of the spine in *syringomyelia*.

RADIUM

Our knowledge of the action of radium is derived from the study of its salts, the element itself having not yet been isolated. It gives out three distinct kinds of rays—alpha, beta, and gamma rays—which are affected differently by the action of a magnet, but all of which penetrate substances opaque to ordinary light and all of which produce chemic, electric, photographic, and physiologic effects. Enclosed in an air-tight container of metal, glass, or rubber the salts retain radio-activity unchanged for an indefinite period.

The emanation of radium produces physiologic effects similar to those produced by x-rays, and the therapeutic uses of the former follow the same lines as those of the latter. However, in some conditions one activity yields better results than the other. For use in cavities, such as the uterus, rectum, bladder, mouth and esophagus, radium therapy is more easy of application and is the method of choice. As radium rays are capable of producing untoward effects similar to those resulting from the x-rays, the two forces must be handled with equal care.

Next to radium *mesothorium* is the most important radio-active substance. It costs much less than pure radium salts, but is apparently less powerful. Many natural spring waters also contain radiferous substances. Such waters, as well as solutions in which radio-activity has been induced by the absorption of the emanation of radium, have been used both internally and externally in various diseases, such as *gout*, *chronic infective arthritis*, *arterial hypertension*, etc., but their value is somewhat doubtful. Mere traces of radio-active substances are certainly useless. It has been shown by chemists in the Department of Agriculture that it would be necessary to consume 2810 gallons

daily of the water yielding the largest quantity of temporary radio-activity in order to obtain the minimal therapeutic dose.

ACTINOTHERAPY

The method devised by Finsen of treating certain localized diseases of the skin by means of concentrated rays of either sunlight or electric arc-light has met with considerable success. It is based upon three postulates proved experimentally by Widmark, Finsen, Bie, and Godneff: The power of the chemical rays to penetrate the skin; the bactericidal properties of these rays; and the power of the chemical rays to excite an inflammatory reaction in the skin. Finsen's apparatus is constructed to accomplish the following objects: To concentrate the light, to absorb or to exclude most of the heat-rays (ultra-red, red, and yellow) without impairing the chemical rays (ultra-violet, violet, and blue), to keep the skin cool, and to render the tissues anemic. The last is necessary to secure penetration of the chemical rays.

The apparatus for sunlight consists of a lens from 8 to 15 inches (20.0–40.0 cm.) in diameter. This lens is composed of two glasses, one curved and the other plain, adjusted in a brass ring and separated from each other by a weak ammoniacal solution of copper sulphate. The blue liquid does not affect the chemical rays, but it cools the light by arresting the heat-rays. The apparatus for sunlight consists of two quartz lenses framed in two brass tubes, which can be moved the one into the other, like the two pieces of a telescope. The lenses are separated from each other by a space filled with distilled water, and in order to prevent overheating of the latter by the absorption of the ultra-red rays cold water is made to circulate through a mantle surrounding this section of the tube. In both plans heating of the skin is further avoided by making cold water run through a hollow quartz lens, which is applied to the affected part with sufficient pressure to make the tissues anemic.

Several modifications of the Finsen lamp, as the Kromayer quartz mercury-vacuum lamp, the Heraeus quartz light, and the Alpine Sun Lamp, are in use.

Good results have been achieved with the Finsen method in *lupus vulgaris*, *epithelioma of the skin*, *lupus erythematosus*, and *alopecia areata*. Relapses are said to be rare, and the applications are painless. Apart from the cumbersomeness of the apparatus and the necessity of trained assistants, the main drawback to the Finsen treatment is its duration. Daily sittings, each lasting an hour, are required for periods ranging from several weeks to a year, or more.

Direct sun rays (*heliotherapy*) have been shown to be of considerable value, in conjunction with other approved measures, in the treatment of *tuberculosis, especially of the bones, joints, and skin*, in *rickets*, in *anemia*, and in certain *diseases of the skin*. The rays may be applied to the part affected or to the whole body. In either case the skin should be bare, although the head must always be protected. When the whole body is to be treated, individual parts should first be exposed and the duration of the baths should be gradually lengthened from ten or fifteen minutes to several hours. The beneficial effects of the sun treatment probably depend largely upon the action of the ultra violet rays, which apparently is closely related to that of radium and the roentgen rays. It is important to bear in mind that the potent waves of short length do not penetrate glass.

APPLIED THERAPEUTICS

THE SPECIFIC INFECTIONS

TYPHOID FEVER

As soon as symptoms of typhoid fever show themselves, even if the diagnosis is in doubt, the patient should be put to bed and kept there until convalescence is well advanced. Hospital treatment offers many advantages, but in many cases it is not essential. It is true, however, "that a good nurse without any doctor is better than the best doctor without any nurse." Whether the treatment is conducted in the home or in the hospital, isolation is essential. Everything that is likely to tire the patient or to disturb his emotions must be avoided, and therefore the fewer the visitors that he sees the better. The room should be large and airy, and provided with efficient means of securing good ventilation. The temperature of the room should be kept between 65° and 70° F. (18.5°–21° C.). The bed should be moderately firm. The mattress should be protected by a rubber cloth spread beneath the sheet and the latter should be kept smooth to guard against the development of bedsores. Even in mild cases it is advisable to have a nurse or attendant constantly at hand, since accidents resulting from sudden delirium are liable to occur. The use of the bed-pan and urinal must be insisted upon from the beginning. Absolute cleanliness is all important.

Stools and other excreta of typhoid patients should be thoroughly mixed with twice their volume of a 5 per cent. phenol solution or a 5 per cent. solution of a good preparation of chlorinated lime and allowed to stand for at least two hours. Disinfection of feces and urine should be continued until the third or fourth week of convalescence or, if possible, until several examinations have shown them to be free from typhoid bacilli. After a stool the patient's buttocks should be carefully washed with a disinfectant solution and the cloths used for the purpose should subsequently be burned. Bed-linen, etc., should be soaked in a solution of phenol (5 per cent.) and boiled before being washed. The patient should have his own eating utensils and these should be disinfected after use by boiling. The disinfection of the bath-water is best accomplished by stirring into it about half a pound of chlorinated lime (250 gm.) and allowing it to stand for an hour.

Throughout the attack the nurse should wear rubber gloves when giving baths or handling otherwise the patient, or afterward wash the hands thoroughly with hot water and soap and then bathe them in 70 per cent. alcohol.

The position of the patient should be changed from time to time, not only to avoid bedsores, but to lessen the tendency to hypostatic congestion of the lungs. Parts that are subjected to pressure should be frequently sponged with alcohol and then freely dusted with talcum powder. After each feeding *the teeth* should be cleaned and the mouth swabbed out with a saturated solution of boric acid or with such a wash as:

R. Succi limonis.....	f ʒi (4.0 mls)
Glycerini.....	f ʒiii (12.0 mls)
Liquoris antiseptici.....	f ʒi (30.0 mls)
Aquæ.....	q. s. ad f ʒvi (180.0 mls).—M.

Heavy coatings on the tongue may be removed by careful scraping with a whalebone bent into a loop.

The *food* should be liquid or semiliquid, nutritious, and easily digestible, the exact quality and quantity depending on the degree of toxemia and the presence or absence of gastro-intestinal disturbances. Milk alone (3 to 4 pints in 24 hours) does not supply more than one-half of the required number of calories (2500), but, as a rule, it should form a large part of the diet. It may be given diluted with lime-water or aerated water, or as buttermilk, malted milk, koumiss, junket, or in part as cream or ice-cream. Among other safe foods may be mentioned raw or soft boiled eggs, strained gruels, milk toast, chicken jelly, tea, cocoa, fruit juices, blanc mange, wine jelly and custard. Beef tea has little caloric value and may even be harmful, but soups of chicken, mutton, veal or oysters, strained and thickened with rice flour are often useful. Three pints of good milk, to which 6 ounces of cream and 6 ounces of milk sugar have been added, together with a soft boiled egg and a dish of rice custard pudding or of strained oatmeal in the twenty-four hours will allow the patient a little more than 2000 calories. If there are signs of gastric disturbance or if diarrhea sets in the diet should be restricted for a time to whey or albumin water.* As a rule, the food should be given in divided quantities every three hours, the patient being aroused at night for nourishment, unless his attack is a very mild one or unless he has recently suffered from insomnia.

* Albumin water is made by shaking together the whites of one or two eggs and a little water, then straining and adding a few drops of orange juice or sherry and, perhaps, some sugar.

Water should be given in large amounts between the feedings, the patient being urged to take it even if he has no desire for it. Taken freely, the water stimulates excretion, improves the condition of the mouth, and lessens the nervous symptoms.

Alcohol is not needed in the majority of cases, but when there is evidence of previous intemperance, when the patient is unable to take enough food, and especially when there are indications of severe toxemia it is often of great value. Ordinarily, the best form of alcohol is whisky or brandy, but occasionally, sherry, port, or champagne may be better borne. At first 1 or 2 ounces (30.0–60.0 mls) of whisky in the twenty-four hours may be sufficient; later it may be necessary to increase the amount to 3 or 4 ounces (90.0–120.0 mls) or more. The quantity must be determined in each case by the effect. If the pulse becomes stronger and less rapid, the tongue less dry, the urine more copious, and the mind clearer under the administration of the alcohol, it is doing good; if, however, opposite effects are observed, it is doing harm, at least in the quantity in which it is being employed.

There is ample evidence to show that the mortality of typhoid fever is considerably reduced by the *cold-bath treatment*, strongly advocated by Brand, of Stettin (see p. 534). To secure the best results, the bathing should be instituted early and continued systematically throughout the attack. Modifications of the procedure are often desirable or absolutely necessary. Thus, if the patient is very nervous the initial bath may be given at 80°, 85° or even 90° F., or throughout he may be bathed in water of about 90° F., which is gradually cooled down to 75° or 70°. Again, in debilitated subjects, or in patients who are already markedly toxic when first seen, it is usually advisable to give shorter baths and to have the temperature of the water higher (75° or 80° F.). The good effects of the cold baths are: Prevention or lessening of nervous symptoms, improvement in the pulse, increased secretion of urine and reduction of temperature. When employed systematically from the beginning, the so-called typhoid state rarely develops. Contraindications to the use of the baths are hemorrhage, indications of intestinal perforation or peritonitis, phlebitis, cholecystitis, great prostration and menstruation. Pneumonia and pregnancy are not contraindications, nor are shivering and cyanosis, unless very prolonged. Collapse, abdominal pain, hemorrhage, vomiting, and extreme cyanosis are indications for immediate removal from the bath.

When for any reason a tub cannot be used a trough may be made in the bed by spreading a large rubber sheet under the patient and elevating its edges on coils of blankets or on sand-bags. When the cold baths are not well borne or cannot con-

veniently be given, cold packs or cold sponging may be employed, although they are much inferior to immersion with friction. In applying the cold pack the bed is first protected by a rubber cloth, and then the patient is stripped and wrapped in a sheet wrung out of water at 70°–60° F. After fifteen or twenty minutes he is rubbed dry. During the pack it is well to sprinkle the sheet with cold water. Cold sponging gives comfort to the patient, but has little effect on the temperature or the general condition. Alcohol may be added to the water, which may be at 65° F. or less, and the sponging may be kept up for ten minutes and be repeated every two hours.

Specific Treatment.—The use of vaccines in the treatment of typhoid fever is still in the experimental stage. Numerous reports on the subject have appeared during the last few years, but the results as shown by the death-rate are not convincing. All observers emphasize the importance of early treatment, and agree that the vaccines, if properly used, at least do no harm. An initial dose of from 250,000,000 to 500,000,000 bacteria (prepared by Wright's method) should be given subcutaneously and followed by two or more larger doses at three-day intervals. Ichikawa has reported striking results from the intravenous injection of sensitized bacteria (a mixture of typhoid bacilli and serum from typhoid convalescents) and Koranyi has confirmed Ichikawa's claims.

Treatment of Special Symptoms and Complications.—

Cardiovascular System.—Cold bathing and the timely use of alcohol do much to guard against heart-failure. When the tendency to cardiac failure is pronounced strychnin may be given in doses of $\frac{1}{40}$ to $\frac{1}{30}$ grain (0.0016–0.002 gm.), subcutaneously or by the mouth, every four hours. Digalen, 10 minims (0.6 mil), or digipuratum, 10 minims (0.6 mil), subcutaneously, three times a day, is sometimes useful. Salt solution (500 to 750 mls) once or twice a day, by the bowel or subcutaneously, is often serviceable. In threatened collapse camphor, 2 grains (0.13 gm.), in sterile olive oil, or caffein and sodium salicylate, 5 grains (0.3 gm.), may be given into a muscle every two or three hours, or epinephrin, 2 to 3 minims (0.1–0.2 mls) may be given intravenously, and followed by the camphor or caffein.

Phlebitis should be treated by rest of the affected limb in an elevated position and the application of cotton-wool and a light bandage. In the early stages an ice-bag over the thrombosis or compresses wrung out of a saturated solution of magnesium sulphate will usually relieve the pain. If there is very severe pain morphin may be required. Later, an ointment of mercury and

belladonna may be used. If the limb swells when the patient is up and about an elastic stocking should be worn.

Nervous System.—Headache is best treated by the use of the ice-cap. Occasionally, a small dose of acetphenetidin, repeated once or twice, may be needed. The general, nervous symptoms are best controlled by hydrotherapy. Muttering usually calls for alcoholic stimulation. In active or violent delirium morphin alone in combination with scopolamin may be necessary. Restraint by sheets is sometimes required. Meningism often yields to lumbar puncture. Wakefulness may usually be overcome by a cold pack at night or by the use of bromids, chloral, trional or barbital in moderate doses. When insomnia is prolonged, however, it is advisable to use morphin hypodermically. For tender toes applications of methyl salicylate with 20 grains (1.3 gm.) of menthol to the ounce (30.0 mls) or light paintings with a mixture of tincture of iodine and alcohol (equal parts) are useful.

Gastro-intestinal Tract.—Vomiting at the outset usually yields to a reduction of the diet to albumin-water or to the temporary suspension of all feeding. The best sedatives are cracked ice, powders of cerium oxalate, 10 grains (0.65 gm.), or of bismuth subnitrate, 10 grains (0.65 gm.), and tablets of cocain, $\frac{1}{6}$ grain (0.01 gm.). A mustard plaster to the epigastrium is sometimes efficacious, and in intractable cases lavage should be tried. If the bowels do not move spontaneously an enema of oil or of soap and water may be given every other day. Except perhaps at the onset, no purgative should be given by the mouth during the febrile period. Diarrhea does not call for intervention unless there are more than 2 or 3 loose stools in the twenty-four hours. In the majority of cases it yields to the temporary substitution of albumin-water for milk and other foods. In some cases, however, it is necessary to give bismuth, 20 to 30 grains (1.3–2.0 gm.) with codein and an antiseptic, as in the following formula:

R̄.	Codeinæ sulphatis.....	gr. ii–iv (0.13–0.25 gm.)
	Phenylis salicylatis.....	gr. xxiv (1.5 gm.)
	Bismuthi subnitratis.....	℥ss (15.0 gm.).—M.
	Fiant chartulæ No. xii.	
Sig.	—One every three hours.	

In obstinate cases silver nitrate, $\frac{1}{4}$ grain (0.015 gm.), or copper sulphate, $\frac{1}{2}$ grain (0.03 gm.), with opium, in pill will sometimes be found useful.

Tympanites may often be relieved by reducing the diet to albumin-water, applying turpentine stupes or cold water compresses to the abdomen, and giving by the mouth turpentine,

10 minims (0.6 mils) in capsules or in emulsion. Saline irrigations and enemas containing asafetida or turpentine are also useful. If extreme, a soft rectal tube may be introduced into the bowel and left in for 15 or 20 minutes. When all these measures fail, a subcutaneous injection of pituitary extract (1 mil) or of eserine sulphate, $\frac{1}{50}$ grain (0.0013 gm.) may be tried.

Intestinal hemorrhage is best treated by securing absolute rest, withholding food temporarily, applying an ice-bag to the abdomen, and giving morphine hypodermically. Human serum or fresh horse serum (10 to 20 mils) is worthy of trial, especially in repeated or prolonged bleeding. Profound anemia following profuse hemorrhage will call for elevation of the foot of the bed, and the application of compressing bandages to the arms and legs. The administration of stimulants and the subcutaneous or intravenous injection of salt solution should be withheld unless death from collapse is imminent, as they favor a recurrence of the bleeding. Blood transfusion is preferable to the injection of salt solution, and if feasible should be substituted for the latter when filling of the vessels is imperative.

Recovery from perforation is so very rare under expectant treatment that operative intervention should be urged in all cases in which the patient is not obviously moribund. Statistics show a recovery rate of at least 25 per cent. in operations done within the first twenty-four hours.

Urinary Tract.—Retention of urine may frequently be overcome by the use of hot applications to the abdomen or enemas of hot water. In some cases, however, it is necessary to employ the catheter. For bacilluria, hexamethylenamine, 10 to 15 grains (0.65–1.0 gm.) three times a day, is the best remedy.

Respiratory Tract.—The bronchitis, as a rule, may be disregarded. If severe, it will require the administration of expectorants, preferably potassium citrate, 20 grains (1.3 gm.) or ammonium chloride, 5 to 10 grains (0.3–0.6 gm.), three times a day, and, perhaps, small doses of paregoric. Hypostatic pneumonia can be in great measure prevented by hydrotherapy, frequent change of position, and the timely use of stimulants. When developed, it is often relieved by the liberal use of dry cups. Ordinary pneumonia is to be treated as it would be if it were primary.

The Skin.—Bedsore can usually be prevented by absolute cleanliness, attention to the smoothness and dryness of the sheets, judicious changes of position, frequent applications of alcohol and dusting-powder, and the timely use of air-cushions or a water-bed. Congested areas may be painted with a 1 per cent. solution of picric acid. Slight abrasions may be painted with

flexible collodion, or covered with balsam of Peru and then powdered. When there is much difficulty in keeping the parts dry, zinc ointment may be freely applied. Ulcers should be washed with antiseptic solutions, dusted with iodoform or aristol, and then protected by a large piece of soap-plaster. An ointment of balsam of Peru, 2 drams (8.0 gm.); aristol 1 dram (4.0 gm.); and petrolatum, 1 ounce (30.0 gm.), is sometimes very efficacious.

Typhoid Carriers.—No satisfactory means of ridding typhoid carriers of their infection has yet been found. So-called intestinal and urinary antiseptics, such as salol and hexamethylenamin, have been tried, but usually without effecting any permanent benefit. Treatment by autogenous bacterial vaccines seems to offer a slightly better chance of success. In some instances cholecystectomy has given decisive results. Carriers should be under the observation of boards of health and should not be allowed to engage in occupations requiring the handling of food materials.

LOBAR PNEUMONIA

(Croupous Pneumonia)

Absolute rest is imperative and should be enjoined even if there is only a suspicion that pneumonia is developing. The bed pan should be used throughout the attack, and moving the patient for bathing and physical examination should be avoided so far as possible. The number of visitors to the sick-room should be strictly limited. In cases of average severity, without complications, the patient may be allowed to sit up after the temperature has been normal for a week or ten days.

An abundance of *cool fresh air* is essential. The windows of the sick-room should be kept wide open, regardless of atmospheric conditions. Except in the case of very young children, old persons and frail patients, treatment out-of-doors on an open porch or balcony is usually advisable. Screening from drafts, however, is necessary, and in cool weather the patient must be well protected by blankets and suitable underclothing to prevent chilling. Under no circumstances should his body be exposed for bathing or examination in the open air. That the nurse in charge of the patient should be warmly clad is equally important. If the outdoor treatment makes the patient more uncomfortable and more restless, it should not be enforced.

The *food* should be nourishing but easily digestible. Milk, junket, broths, soft boiled eggs, strained oatmeal gruel, custards, blanc mange and calves'-foot jelly are suitable forms of nourish-

ment. Cool water should be given freely between meals. The bowels should be moved regularly, using for the purpose, if necessary, mild laxatives or enemas.

Even if the temperature is not high, *hydrotherapy*, especially cold sponging, is of service, provided it can be carried out with causing much disturbance of the patient. The use of tub-baths or packs is rarely advisable. Except for the purpose of combating certain symptoms, *local applications* are useless. If there are no special indications the chest may be enveloped in a light padded jacket.

Specific Treatment.—Workers in the Rockefeller Institute have demonstrated that in pneumonia due to pneumococcus of Type I, which is responsible for about $\frac{1}{3}$ of all cases, homologous immune horse-serum is highly effective, especially if used early in the disease, reducing the mortality to about 7 per cent. Homologous serums in pneumonia due to other types of pneumococci are much less efficacious and polyvalent serums are of doubtful value. The usual dose of serum is 90 to 100 mils, preferably diluted with salt solution, intravenously, every eight hours until a definite effect has been obtained. The danger of anaphylactic shock may be reduced to a minimum by injecting subcutaneously 0.5 to 1 mil of horse serum an hour before the serum treatment and by administering the serum very slowly especially at first (15 minutes for the first 15 mils).

Stengel reports very encouraging results from intravenous injections (30 mils) of blood-serum obtained from pneumonia patients just following the crisis. A serum-free solution of pneumococcus antibodies has recently been used with some success (see p. 471). Favorable results have also been reported from intravenous injections of non-specific proteins, but this treatment produces severe reactions.

Symptomatic Treatment. *Pleuritic Pain.*—In many cases this may be relieved by the application of a mustard plaster, turpentine stupe or ice-bag. The use of a few wet or dry cups is still more effective. If the pain is very severe, morphin should be given hypodermically.

Cough.—Frequent and unproductive cough is best controlled by codein in doses of $\frac{1}{8}$ to $\frac{1}{6}$ grain (0.008–0.01 gm.) by the mouth or by small doses of morphin hypodermically. Expectorants are not usually needed. If, however, there is much bronchial catarrh and the expectoration is very viscid ammonium chlorid or potassium citrate may be of service.

Circulatory Failure.—The use of circulatory stimulants as a routine measure is probably better avoided. Cole and other workers in the Rockefeller Institute, however, recommend the

administration of digipuratum (8 gr.—0.5 gm. a day by the mouth), or a corresponding dose of some other preparation of digitalis, for a period of two days. The purpose of this early administration of the drug is not to produce immediate effects upon the heart, but to put the patient into such a condition that later if need arises physiologic digitalis effects may quickly be obtained by the administration of small doses by the mouth. Whether digitalis is used from the beginning or not, it is indicated when the pulse becomes unusually accelerated and weak. If it fails caffein or strychnin may be used as an adjuvant or as a substitute. These two drugs are useful also in combating respiratory depression, which is sometimes responsible for circulatory failure. Alcohol, as a rule, is better avoided, unless there is an alcoholic history, and even then it should be used only in moderate amounts, that is to the extent of about 3 or 4 ounces in the twenty-four hours. Atropin is often of value when there is excessive bronchial secretion or a tendency to pulmonary edema.

In acute heart failure an intravenous injection of strophanthin ($\frac{1}{80}$ gr.—0.00075 gm.) is sometimes very effective, but under no circumstances should this treatment be employed if the patient has been taking digitalis. If strophanthin cannot be given, camphor (2 gr.—0.13 gm.—in sterile olive oil every two hours) or epinephrin (15–30 min. — 1–2 mils in saline solution and very slowly administered) should be tried. In cases with embarrassment of the right ventricle, as shown by great cyanosis and extension of the area of heart dulness toward the right, moderate venesection is indicated. Oxygen makes the breathing somewhat easier and to this extent aids in conserving energy.

Insomnia.—In the early stages of the disease, morphin is beneficial and safe. Later, preference should be given, as a rule, to bromids, chloral or barbital.

Abdominal Distention.—In the milder cases the application of turpentine stupes, and the use of asafetida enemas usually suffice. Hot saline solution by proctoclysis is sometimes useful. The introduction of a rectal tube may also prove effective. In severe cases pituitary extract (15 min.—1 mil, subcutaneously, every two hours), or physostigmin salicylate ($\frac{1}{60}$ gr.—0.001 gm. subcutaneously, and repeated in three hours) often affords temporary relief.

CEREBROSPINAL FEVER

(Cerebrospinal Meningitis)

The sick-room should be quiet, darkened, and well-ventilated. The diet should be light but supporting. Occasionally, in order

to secure the ingestion of sufficient nourishment, it may be necessary to feed the patient by means of a stomach tube. The bowels should be opened freely at the onset, preferably by calomel, and then every day or two by a cascara preparation, milk of magnesia, solution of magnesium citrate, or a laxative mineral water.

The specific treatment, which consists in the use of a polyvalent antimeningococcus serum, prepared after the method of Jochmann, Flexner and Jobling and others has apparently reduced the mortality of the disease about one-half. Of 1394 cases treated with serum in the Texas epidemic of 1912 the mortality was 37 per cent., as compared with a mortality of 77 per cent. among 562 cases treated without serum (Sophian). The earlier in the case the serum is used, the better are the results. According to Flexner, of 199 cases treated in the first three days the mortality was only 18.1 per cent. The dose of serum for adults is from 30 to 50 mils, and for infants and children 5 to 20 mils, the amount varying with the quantity of cerebrospinal fluid withdrawn. In children, especially, the dose should be a few mils less than the amount of fluid removed. When only a small amount of cerebrospinal fluid is obtained, not more than 10 mils should be injected. In cases of moderate severity the injections should be given every day for 3 or 4 days and then every other day until the patient's general condition and the result of the examination of the cerebrospinal fluid indicate that the infection has subsided. If the case is severe and not seen until after the third day the first injections should be given every 12 hours. The average case requires in all from 4 to 8 injections. The serum should always be introduced slowly and preferably by the gravity method. If symptoms of collapse appear some of the fluid should be allowed to escape through the needle. Artificial respiration and an injection of atropin sulphate— $\frac{1}{100}$ to $\frac{1}{60}$ grain (0.00065–0.001 gm.)—may also be required.

When the patient is seen early and bacteremia can be demonstrated the serum may be given also intravenously, although with this method of administration there are likely to be severe systemic reactions, especially in children. The dose of serum for intravenous injection is from 30 to 120 mils daily for several days, the amount depending upon the age of the patient and the severity of the attack. The injection should always be made very slowly and to avoid serious reactions, it is advisable to desensitize the patient first by giving an hour before the intravenous injection 1 mil of the serum subcutaneously.

Apart from the use of specific serum the treatment is chiefly symptomatic. For headache, restlessness, delirium, insomnia, etc. morphin or code in, preferably hypodermically, is often required.

Bromids, phenobarbital, sulphonal, etc. are not usually effective. The application of an ice-cap to the head is helpful. Hot baths (105°–110° F.), once or twice a day, for from 5 to 15 minutes, are often of value. If a circulatory stimulant is required, digitalis should be chosen, as strychnin and caffein are likely to increase the nervous excitability. When there are evidences of increased intraventricular pressure and lumbar puncture affords no relief, the ventricles may be tapped or a suboccipital puncture may be made into the cisterna magna. After tapping, if the fluid is turbid or purulent, a small amount of antimeningococcic serum may be injected into the cavity. Painful joints may be treated locally as in cases of rheumatism. In refractory arthritis the fluid may be removed from the joint and serum injected.

Rest is essential during convalescence and the return to usual activities should always be effected slowly. Tonics, especially iron, are frequently indicated.

ERYSIPELAS

A supporting liquid or semi-liquid diet is required. High fever is best controlled by cold sponging or the cold pack. Restlessness, delirium and insomnia call for the application of an ice-bag to the head and the administration of bromids or chloral. Digitalis, caffein and strychnin are the most reliable remedies in combating circulatory weakness. Of the special remedies that have been recommended from time to time, ferric chlorid, first suggested by Bell in 1851, has remained the longest in favor. From 10 to 20 minims (0.6–1.2 mls) may be given every three hours. While it is apparently of some service, the drug is by no means a specific and should be withdrawn if it disturbs digestion.

Local Treatment.—The most useful local applications are lotions of ice-cold lead-water and laudanum, of a saturated solution of magnesium sulphate, and of a saturated solution of boric acid, and ointments of ichthyol 30 to 40 per cent. and of colloidal silver (Unguentum Crédé—15 per cent.). The following ointment suggested by Roswell Park often acts favorably:

R. Ichthyol.....	gr. xxx–xl (2.0–2.6 gm.)
Resorcinolis.....	℥ss (2.0 gm.)
Unguenti hydrargyri.....	℥iv (15.0 gm.)
Adipis lanæ hydrosi.....	℥v (20.0 gm.).—M.

The application of lunar caustic in a ring or of iodine in a broad band about two inches in advance of the inflamed area sometimes arrests the spread of the disease in migratory erysipelas, but more frequently it is unsuccessful.

Local abscesses should be treated surgically. Should the larynx become involved, the constant sucking of ice may control the swelling, but if this measure fails and dyspnea becomes pronounced recourse should be had to scarification of the edematous tissue, tracheotomy or intubation.

SEPTICEMIA; SEPTICOPYEMIA

The chief indications are to evacuate and drain all suppurative foci that are accessible and to conserve the strength of the patient by good hygienic conditions, careful nursing, and a liberal supply of nutritious, easily assimilated food. Water should be used freely. If it cannot be taken by the mouth in sufficient quantity, it should be given in the form of normal saline solution by rectal, subcutaneous or intravenous injection. Alcohol in moderate amounts is undoubtedly of value. Quinin in tonic doses is apparently of service. Strychnin and digitalis may be required to ward off threatened collapse. The fever is best controlled by cold sponging. Coal-tar antipyretics should not be employed. Morphine may have to be given for pain or insomnia.

Intravenous injections of Credé's colloid silver, of formaldehyde, or other antiseptics have not yielded encouraging results. In acute streptococcus infections antistreptococcus serum, if properly administered, is harmless and sometimes seems to be efficacious, especially if used early and in large doses. To obtain the best results the serum should be polyvalent and should be given intravenously or intramuscularly. In severe cases from 50 to 100 mls should be given at once and repeated in from 12 to 24 hours. In streptococcus endocarditis, the results, on the whole, have been unfavorable. Regarding staphylococcus infections, no satisfactory serum has yet been prepared. In acute septicemia vaccines are rarely beneficial, but in the more chronic infections, they may be of considerable value in conjunction with appropriate surgical treatment. Stock vaccines may be used, although autogenous vaccines are likely to yield better results.

TETANUS

With the appearance of the first signs of the disease the patient should be placed in a darkened, well-ventilated and quiet room, and protected, as far as possible, from all external irritations. The bowels should be moved by salines or castor oil or by enemata. Retention of urine not rarely occurs and requires the use of the catheter. The food should be nutritious, but readily digestible. If swallowing is not possible, food must be introduced into the

stomach through a nasal tube passed under chloroform anesthesia. If necessary, proctoclysis with normal salt solution is thought to be of service.

The curative power of antitetanic serum is much less certain than its usefulness as a means of prophylaxis, nevertheless most observers believe that it is of value when used promptly and in large doses. It is best administered intrathecally and subcutaneously or intramuscularly. Intravenous injection has had its advocates, but it has been largely discarded on account of the great risk of anaphylaxis. Intraneural administration is also recommended and is a rational measure, especially when localized rigidity is an early sign. At least 3000 units should be injected intrathecally, after removal of a requisite amount of cerebrospinal fluid, and the treatment should be repeated daily for 4 or 5 days. At the same time from 10,000 to 25,000 units should be administered intramuscularly or subcutaneously, and, unless improvement occurs and is sustained, a similar amount should be injected again in from 18 to 24 hours. The drawback to subcutaneous and intramuscular injections is the extreme slowness of absorption. In cases of ascending tetanus from 500 to 1500 units may be injected into the main nerve-trunk. Baccelli's treatment, which consists in administering intramuscularly 1 mil of a 1 per cent. solution of phenol every few hours, until 40 to 70 mils in all are given daily, has not met with much favor in the United States or in England (see Memorandum on Tetanus, issued by the British War Office*).

Symptomatic treatment is always required to control the spasms and to secure rest and sleep. The best drugs for the purpose are chloral and bromids, the former in doses of 30 to 40 grains (2.0–2.6 gm.) every 6 hours, and the latter in doses of 1 dram (4.0 gm.), every 6 hours. Chorbutoanol (chloretone) and scopolamin (hyoscin) have also been recommended, but they must be used very cautiously. Morphin is of service when there is severe pain and insomnia. It should not be employed, however, to the exclusion of chloral and bromids. The intraspinal injection of a 25 per cent. solution of magnesium sulphate (1 mil for every 20 pounds of body-weight) has been employed to some extent as a means of depressing the spinal cord, but in a number of instances it has caused an alarming depression of respiration. If the paroxysms are so violent that they threaten death by asphyxia or exhaustion, chloroform inhalations should be used. Stimulants (digitalis, caffen, camphor) are frequently required to combat exhaustion and circulatory failure.

* Brit. Med. Jour., Nov. 11, 1916.

DIPHTHERIA

The sick-room should be well ventilated and the temperature maintained at about 68° F. In laryngeal cases it is desirable to have the atmosphere moist and this may be accomplished by generating steam in a croup-kettle or in an ordinary kettle. Absolute rest must be enforced. Even in mild cases the patient should not leave the bed for at least three weeks and if there have been signs of cardiac failure or of paralysis the period of inactivity should be much longer. The diet should consist of bland, nutritious, liquid or semi-liquid foods. Milk, junket, ice-cream, soft boiled eggs, animal broths, gelatin, and gruels are suitable forms of nourishment. If sufficient nutriment cannot be swallowed recourse must be had to gavage or to rectal feeding. Cool water should be given freely. The bowels should be opened at the beginning of the attack, preferably by calomel, followed by milk of magnesia or magnesia citrate, and kept open throughout the illness by laxatives or the use of enemas.

Statistical reports from all parts of the world during the last 25 years prove conclusively that the one remedy of great value in the treatment of diphtheria is the blood-serum of a horse that has been immunized by a series of injections of diphtheria toxin. This serum, or antitoxin, as it is commonly called, neutralizes the toxin of the disease and apparently aids in destroying the bacilli, probably by favoring phagocytosis (Kolmer). It should be used at the earliest moment possible and in suspicious cases at once without waiting for a report of the culture. The dose varies with the location and extent of the lesion, the degree of toxemia, the day of the disease when treatment is begun, and the age of the patient. In cases of faucial or tonsillar diphtheria which are of moderate severity and which are first seen on the second day, the initial dose should not be less than 10,000 units. If the patient is seen on the first day and the patch is small and confined to one tonsil, 5000 units will usually suffice. In laryngeal diphtheria the dose should be from 10,000 to 20,000 units according to the time at which treatment is instituted. In well-marked nasal diphtheria, unless the patient is seen very early, the dose should not be less than 15,000 units. Age need only be considered in the case of young children under 2 years, and in them the dose should be about one-half of that required for older persons. Unless there is a very definite improvement, as shown by the appearance of the throat and the patient's general condition, the treatment should be repeated in 12 hours. In severe cases, if no improvement is observed, a second and larger should be given in 6 hours. In some cases it is necessary to administer 3,

4 or more doses of antitoxin, and to use in the aggregate from 50,000 to 100,000 units. The danger lies not in using too much, but in using too little.

Except in malignant or profoundly toxic cases, when it may be given intravenously, antitoxin should be injected subcutaneously or intramuscularly, preferably in the pectoral region, abdominal wall, or flank. The injections should be made under aseptic precautions. If there is any reason to suspect that the patient is sensitized to horse serum, the physician may inject 0.5 mil of antitoxin for the purpose of producing anti-anaphylaxis, and 2 or 3 hours later administer the remainder of the requisite dose. If anaphylaxis does occur it should be treated by injections of atropin and morphin and, if necessary, by artificial respiration.

Apart from the use of antitoxin, the internal treatment of diphtheria is entirely symptomatic. Caffein, strychnin, digitalis and camphor are frequently required to combat circulatory failure. To secure rest and relieve distress, morphin, in small doses, is sometimes a very useful adjuvant to cardiac stimulants. Proctoclysis with hot normal salt solution may be of value when collapse seems imminent. Notwithstanding the fact that much has been written against the use of alcohol, many clinicians of large experience believe that this drug is decidedly useful when asthenia is pronounced. For a child of 3 or 4 years a dram (4.0 mils) may be given every 3 or 4 hours.

Local Treatment.—Local treatment is of value in securing cleanliness of the affected parts. It cannot destroy the bacteria. Applications should be made with the utmost gentleness and should be unirritating. If they cause violent struggling and exhaust the child it is better to omit them. Irrigation is preferable to spraying, gargling or swabbing. The nozzle of the irrigator should be blunt and covered with soft rubber, and the nurse should be instructed to introduce it gently in a horizontal direction. In both nasal and pharyngeal diphtheria, if the child cannot be raised, the fluid may be poured into the nose from a spoon or better from a nasal cup (Jacobi). Among the best irrigating fluids are hot (100°–105° F.) normal salt solution, Dobell's solution, diluted 3 or 4 times, and boric acid solution (2 per cent.). Externally, hot or cold applications to the throat, whichever may be more grateful to the patient, are sometimes of service. Small pieces of ice held in the mouth tend to relieve soreness and dysphagia. In laryngeal diphtheria when dyspnea becomes marked and recession of the suprasternal and infrasternal regions occurs with each inspiration intubation or tracheotomy is indicated. *Intubation* is usually given the preference, but *tracheotomy* may be required after intubation has

been tried and has failed to remove the obstruction, owing to excessive edema of the fauces or to the presence of membrane below the tube.

Paralysis.—If the soft palate and pharynx are affected and swallowing becomes difficult or impossible recourse must be had temporarily to gavage. Strychnin, $\frac{1}{100}$ grain (0.00065 gm.) three times a day, at 4 years, is useful. In paralysis of the muscles of the neck, shoulders or limbs massage and electricity may also be of service.

Convalescence must be managed with special care on account of the tendency to cardiac failure. Anemia, a common sequel, will require a nutritious diet, and the use of tonics, especially iron.

INFLUENZA

The most important features of the treatment are immediate and complete rest in bed, an abundance of fresh air without draft, a liberal diet of easily digestible food, and attentive, skillful nursing. Owing to the possibility of relapse and complications, especially pneumonia, the rest should be maintained for at least a week after the fever and other symptoms have entirely disappeared. The bowel should be moved freely at the onset, preferably by calomel and a saline, and should be kept open throughout the attack. Water should be given in abundance.

In mild cases a hot foot-bath and the administration every 3 hours of an alkaline diuretic, such as the official solution of potassium citrate (4 drams—15.0 mls), and of a moderate dose of Dover's powder (5 grains—0.3 gm.) at night, for 2 or 3 nights, will suffice. For the relief of pains in the head, back and limbs moderate doses of acetylsalicylic acid or of acetphenetidin are useful. Although some prejudice exists against these drugs, they promote comfort and very rarely do harm, unless given in large doses or for long periods. A combination such as the following is often satisfactory:

℞. Codeinæ sulphatis..... gr. ii (0.13 gm.)
 Acetphenetidini
 Acidi acetylsalicylici..... āā gr. xl (2.5 gm.)—M.
 Pone in capsulas No. xii.

Sig.—One every three hours.

Or,

℞. Acetphenetidini..... gr. xl (2.5 gm.)
 Sodii benzoatis..... ʒi (4.0 gm.)—M.

Fiant chartulæ No. xii.

Sig.—One every three hours.

As a rule, analgesics of this class should not be continued beyond the second day. Excessive cough is best controlled by codein in

full doses, or morphin ($\frac{1}{6}$ gr.—0.01 gm.), and the application of sinapisms or of dry cups to the chest. Spasmodic cough is sometimes favorably influenced by impregnating the air of the room with steam of a croup kettle which contains a dram or two (4.0–8.0 mils) of compound tincture of benzoin or eucalyptol or 30 minims (2.0 mils) of creosote to each quart of water.

With the first appreciable evidence of circulatory weakness, it is advisable to give digitalis by the mouth or intramuscularly. If the toxemia is profound, caffein in doses of from 1 to 2 grains (0.06–0.13 gm.) three or four times a day, may be used as an adjuvant to digitalis. Proctoclysis with normal salt solution or a 5 per cent. solution of glucose is sometimes helpful.

In threatened collapse, with signs of pulmonary edema, intramuscular injections of camphor should be tried. From 1 to 2 grains (0.065–0.13 gm.) of the drug in oil may be given every 2 or 3 hours. Atropin ($\frac{1}{100}$ gr.—0.0006 gm.), repeated two or three times, at intervals of 2 hours may also be given. For pronounced insomnia bromids or barbital may be tried, but, usually, morphin is the only satisfactory remedy.

Convalescence should be carefully guarded. After severe attacks the patient should abstain from undue activity for 2 or 3 weeks or longer. Tonics are usually indicated. Change of air and scene materially help in restoring strength and overcoming the peculiar mental depression.

BACILLARY DYSENTERY

In the treatment of acute cases absolute rest in bed is imperative. The diet should consist of milk diluted with barley-water, peptonized milk, infant foods, egg albumin, chicken broth and milk toast. In the more chronic cases soft boiled eggs, pulled bread, steamed rice, oysters, tender meats, wine jelly and custard may be allowed. An unirritating purgative (magnesium sulphate, castor oil or calomel) is indicated at the onset. After the free purgation, opium should be given to lessen the colic and tenesmus. It may be administered hypodermically in the form of morphin, or by the stomach or bowel. Turpentine stupes or sinapisms over the abdomen are useful. Tenesmus may also be relieved by ice suppositories, injections of warm mucilage of starch (1 oz.—30.0 mils) of cocain solution (10 min.—0.6 mil of a 4 per cent. solution), or irrigations with normal saline solution. In the subacute and chronic forms irrigations with solutions of silver nitrate (5 grains gradually increased to 20 grains to the pint—0.3–1.3 gm.—to 0.5 L.) are sometimes efficacious. These should be given once a day, the fluid being introduced

very slowly by means of a fountain syringe, with the patient in the dorsal position and with the hips well elevated. Internally, bismuth subcarbonate, 30 grains (2.0 gm.) every 3 hours, with a dose of castor oil or salts every fourth day, is often efficacious. Antitoxic serums seem to have been of service in some outbreaks. If the exact type of infection is not known a polyvalent serum should be used. As the standard of strength of the different preparations varies, the physician must be guided in the matter of dosage by the printed directions accompanying the package. The average dose for an adult is 20 mils, repeated in from 12 to 24 hours if necessary. In severe cases from 50 to 100 mils may be given intravenously. For collapse, stimulants and subcutaneous or intravenous injections of saline solution may be used. In chronic cases change of climate is a valuable aid, and sometimes does more for the patient than all other therapeutic measures.

CHOLERA

From the first appearance of diarrhea the patient should be put to bed and warmly covered. Hot stupes may be applied to the abdomen. Food, other than barley water or whey, which should be given freely, is better avoided. The use of cathartics, even of calomel in fractional doses, is inadvisable, and this is probably true also of opium in any form, although some authorities believe that in the first stage, if there is much discomfort, morphin may be given hypodermically in small doses without risk. There is no specific treatment. Anticholera serum has been used, but without success. Rogers speaks favorably of atropin and potassium permanganate. The former is given hypodermically, morning and evening, in doses of $\frac{1}{100}$ grain (0.0006 gm.), and the latter by the mouth, in pills made up with kaolin and petrolatum, and preferably coated with salol or keratin, the dose being 2 pills, each containing 2 grains (0.13 gm.) of the permanganate, every quarter of an hour for 2 to 4 hours, in accordance with the severity of the case, and then two every half hour until the stools change to green or yellow and become comparatively small.

Collapse is best combated by intravenous injections of normal salt solution every few hours, the fluid being introduced slowly until a full pulse has returned. The amount of fluid usually required for each injection is from 1 to 2 quarts (1.0–2.0 L.). The temperature of the fluid should be about 98° F., or lower, if the patient's rectal temperature is high. Proctoclysis is much

less effective, but it is useful in supplementing the intravenous injections. Other measures useful in collapse include applications of hot blankets and hot water bottles and the administration intramuscularly of caffeine, sodium benzoate, camphor, and pituitary extract. Rogers, who has had a large experience in the treatment of cholera, states that hypertonic salt solution is much superior to normal solution in the stage of collapse when the blood pressure is not over 70 mm. and the specific gravity of the blood is 1.063 or over. He uses a solution containing 120 grains (8.0 gm.) of sodium chlorid and 4 grains (0.26 gm.) of calcium chlorid to the pint (0.5 L.), and injects 3, 4, 5, or even 6 pints, according as the specific gravity of the blood is 1.063, 1.064, 1.065, or 1.066 in male adults and correspondingly less in females and children, in proportion to their approximate weights. Unless the rectal temperature is below 99° F. the solution should never be injected at above blood heat for fear of producing hyperpyrexia, and if the rectal temperature is 100° F. or over the fluid should be given at a temperature between 80° and 90° F. He further advises that normal salt solution should also be given by the rectum, half a pint (250.0 mls) every 2 hours, until the collapse stage is passed and urine is being secreted regularly, and then every 4 hours, until 2 pints of urine are passed in the 24 hours.

In suppression of urine the most promising measures are dry cupping over the kidneys and intravenous and rectal injections of salt solution or, as the anuria is always accompanied by marked acidosis, by intravenous and rectal injections of a 2 per cent. solution of sodium bicarbonate. Sellars has found the alkaline solution just as efficacious in relieving collapse as the salt solution. To allay thirst, cracked ice or iced Seltzer water may be given at frequent intervals. The painful cramps are best treated by warm applications or gentle friction with anodyne liniments. In hyperpyrexia cold sponging and rectal injections of cold water should be tried. Antipyretic drugs should be avoided.

In the stage of reaction liquid foods in small quantities are permissible. Milk with lime-water, whey, thin gruels, albumin-water and light broths are the most appropriate. The return to ordinary foods should be effected very gradually. Water should be given freely, since it tends to restore vascular fulness and favors diuresis. Any tendency to recurrent diarrhea should be met by the administration of bismuth subnitrate or bismuth subsalicylate. Bitter tonics are often of service during convalescence. Change of air is a valuable aid to the restoration of health.

ANTHRAX

Opinions differ as to the advisability of radical local treatment in cutaneous anthrax. Some surgeons advise against excision of the specific lesions contending that it favors rather than hinders the spread of the disease. On the other hand many surgeons, probably the majority, believe that better results are secured by immediately excising the local focus of infection, swabbing the wound with pure phenol and then dressing it with hot antiseptic fomentations, or, if ablation is not feasible, by making crucial incisions into the infected area, treating the wounds with phenol, chlorin solution or tincture of iodine, and then dressing the part with hot antiseptic fomentations. Injections of diluted phenol (5 per cent.) at many points around the focus of infection are also recommended.

Whatever local treatment is employed, Sclavo's antianthrax serum should be given intramuscularly or intravenously, in doses of 50 to 150 mls, and repeated in 24 hours, if there is no improvement. In 164 cases in Italians treated by Sclavo with serum the mortality was only 6 per cent., in contrast to 24 per cent., the rate of all cases treated in Italy over a period of 15 years (Legge). Graham and Regan report very favorably upon injections of antianthrax serum into the indurated border of the pustule as an adjuvant to the employment of serum intravenously and to the exclusion of excision. A total dose of 10 mls may be injected two or three times in the 24 hours, the needle being inserted at two or three points. Kraus, chief bacteriologist of the National Department of Health, Argentina, has recently reported a mortality of only 5 per cent. in 200 cases treated by intramuscular or intravenous injections of normal beef serum (30 to 50 mls, repeated in 12, 24, or 36 hours, as the case required). The serum is heated twice for half an hour at 56°C. before injection. Kolmer, however, has found beef serum without demonstrable protective or curative value in experimental anthrax infections in mice and rabbits. The general supporting treatment recommended in other grave infections is required in all cases of anthrax.

TUBERCULOSIS

Persons with a predisposition to tuberculosis can do much to increase their powers of resistance by strict attention to hygiene. Fresh air, a healthy residence, an outdoor occupation, the wearing of warm clothes, with flannel next to the skin, a diet of wholesome and nutritious food, temperate living, systematic exercise and daily sponging followed by friction of the skin are the factors

to be relied upon in attempting to overcome individual susceptibility. Persons recovering from such diseases as pleurisy, bronchopneumonia, whooping-cough, measles and influenza should be treated with the utmost care. As enlarged tonsils, adenoid growths, and other obstructions in the upper air-passages interfere with free respiration and increase the risk of infection, they should be removed. Finally, all local foci of tuberculosis, such as frequently appear in the cervical lymph-nodes, joints and bones, should receive immediate attention.

Tuberculous patients should be taught to hold a cloth before the mouth when coughing and to expectorate only into proper receptacles containing a disinfectant solution (5 per cent. carbolic acid) or into moistened rags or paper napkins, that should be deposited in paper bags and burned before the sputum becomes dry. They should sleep alone. Their rooms should be sunny, well ventilated, and kept scrupulously clean. Consumptives must not be kissed on the lips. The marriage of tuberculous patients should be discouraged, unless the disease has been completely arrested and symptoms have been absent for at least a year, or preferably for two years. Under no circumstances should a tuberculous mother be permitted to suckle her offspring, and the contact of infants with tuberculous parents should be avoided as much as possible.

Sanatorium Treatment.—Sanatorium treatment is not indispensable, but it has a great advantage in that it permits of constant medical supervision of the patient. The sanatorium may be located in almost any climate, even within a few miles of a large city, the only requisites being moderate elevation, well-drained soil, abundant sunshine, and protection from strong winds. The chief elements of the treatment are fresh air by day and night, abundance of good nourishing food, and rest or regulated exercise.

In summer not less than 10 or 12 hours and in winter not less than six or seven hours should be spent out-of-doors. In Falkenstein the patients remain out-of-doors in their chairs from 7 to 10 hours a day all the year round, despite fog, rain or snow and even with the thermometer at 12° C. below zero. Of course, they are sheltered from the wind and rain, and are well-covered with blankets or fur robes. The bed-room windows are kept open during both winter and summer. As a rule, patients soon accustom themselves to live in a low temperature without discomfort.

When digestion is good the patient is given an ordinary diet of wholesome food and encouraged to eat as heartily as his digestive powers will permit. Milk, eggs, beef, mutton, fish, fowl, fresh

vegetables, cereals and fruits are considered suitable forms of nourishment. Pastry, fried foods, coarse vegetables, and sweets are forbidden. As a rule, the meals are given more frequently than in health. Thus, before rising the patient may take hot milk, cocoa or gruel; at breakfast—beef-steak, chops, fish or eggs and bacon, bread and butter, and coffee or milk; at the mid-day meal—soup, fish, meat and vegetables, salad and simple pudding or fruit; at supper—cold meat, bread and butter, cocoa and fresh or preserved fruit; at bed-time a glass of hot milk or an egg-nog. If a sufficient amount of varied food cannot be taken to bring about a gain of from 1 to 2 pounds per week in the body-weight, the daily dietary should be made to include from 3 to 4 pints of milk and from 4 to 6 eggs (raw or cooked). The extra nourishment is best given, as a rule, between meals and on going to bed. If necessary, the milk and eggs may be variously flavored and may be discontinued for a day or two from time to time. Fats—cream, butter and olive oil—if well borne, are valuable. Cod-liver oil, though less used than formerly, is also of service. It is best given 2 hours after a meal, and at first the dose should not exceed a teaspoonful. Digestive disturbance and high fever are contraindications. In every case both the diet and the quantity of food must be controlled by the patient's digestive power and weight. A diet containing more than 3000 calories is not required and may actually prove harmful. Occasionally, anorexia is so pronounced that forced feeding is necessary, but usually the patient can be persuaded to eat, especially if the food is presented to him in an appetizing form. Under the influence of fresh air and rest the appetite often returns with remarkable rapidity.

If the disease is active, that is, if the temperature at any time of the day is above 99.5° or 100° F., if the pulse-rate exceeds 90 per minute, or if the body-weight is decreasing, rest is imperative. If the patient is not too ill to be kept in bed, he may lie for most of the day on a couch in the open air, warmth being maintained by abundant covering and, if necessary, by a hot stone placed at the feet. Under any circumstances absolute rest for a few weeks at the beginning of treatment is advisable, and rest for half an hour before and after meals should always be insisted on, when it is possible. As soon as the disease becomes inactive graded exercise in the open air is indicated. Except for vigorous patients, walking, first on the level and later up inclines, is the safest form of exercise. In many cases, however, calisthenics and various sorts of light out-door work may be permitted. Whatever its form, exercise should always stop short of causing exhaustion and must be lessened or aban-

done if it causes fever or undue acceleration of pulse, or if it impairs the appetite.

A few weeks' residence in a sanatorium is of value even if it only serves to train the patient in the ways of the open-air treatment, but lasting benefit is rarely secured in less than three months and, except in very early cases, permanent arrest should not be expected in less than 2 years.

Climatic Treatment.—Since the open-air treatment of tuberculosis has been shown to be about equally successful in nearly all localities, a change of climate has become a matter of secondary importance. Still, there are some patients, with ample means at their disposal, to whom a protracted stay in a sanatorium would become irksome and distasteful. For such patients prolonged residence in a favorable climate is often of great value. The requisites of a suitable climate are purity of atmosphere, an abundance of sunshine, a dry porous soil, and freedom from high winds and dust. The age of the patient, the extent and type of the disease, and the condition of the other organs must be carefully considered in deciding the questions of altitude, of temperature, and of humidity. Other matters that should not be overlooked in choosing a locality are wholesome food in abundance, good accommodations, and available medical advice. Many young persons, with considerable constitutional vigor, who have but a small area of lung involved, do well in high altitudes, such as are found in Colorado, Wyoming and Montana, and in Switzerland (Davos, Arosa, St. Moritz). Other patients in the early stages seem to do better in resorts at moderate altitudes (1500 to 2500 feet), such as those of the Adirondacks, Asheville, and the Muskoka region. Patients with cardiac disease, pronounced emphysema, diabetes and nephritis, and persons of advanced ages are unsuitable for high altitudes. Tuberculous patients who are elderly, who have advanced lesions, who exhibit pronounced constitutional irritability, or who have emphysema or cardiac, nephritic or arthritic complications do better, as a rule, in mild climates and at low levels, for example at resorts of Southern California or Southern Arizona in this country, or at the Madeira Islands, Algiers, etc., abroad.

A change of climate is contraindicated in acute forms of the disease and in advanced cases of chronic tuberculosis with pronounced symptoms of secondary infection.

Home Treatment.—The vast majority of tuberculous patients are unable to avail themselves of the advantages afforded by a stay in a sanatorium or by residence in a salubrious climate. These may be consoled by the fact that many cases do well at

home when the conditions are not too unfavorable. Treatment at home should be made to imitate as closely as circumstances will permit that which is followed in the sanatorium. The airiest and sunniest room should be selected for the patient. So long as he has fever absolute rest should be insisted upon. During the day, if the weather be element, he should rest on a couch or in a reclining chair in the open air for from 6 to 10 hours, according to the season, and at night sleep with the windows open. As much nourishing food should be supplied as the digestive capacity of the patient will allow. Much stress should be laid on the danger of reinfection, and the patient urged to avoid soiling his hands or clothes with sputum, and always to wash his hands and lips before eating.

Heliotherapy.—Exposure to the rays of the sun apparently has a curative action, and excellent results have been reported, especially in tuberculosis of bones and joints, from exposing the seat of lesion and also other parts of the body to the direct rays and to rays reflected from large mirrors placed near the patient.

Artificial Pneumothorax.—With a careful selection of cases and proper technique, compression and immobilization of the affected lung by the method of Forlanini, which consists in introducing warm nitrogen, oxygen, or sterile air into the pleural cavity, sometimes gives good results. It may be employed in moderately or far-advanced cases in which improvement has not occurred under ordinary methods of treatment and in cases of uncontrollable hemorrhages. The chief contraindications are extensive involvement of both lungs, pleural adhesions or effusion, and serious complications of any kind, especially cardiac or renal disease. As pneumothorax therapy requires close and almost constant observation of the patient, its use should be confined, as a rule, to the hospital or sanatorium. The inflations are made at first every few days and later at intervals of two or three weeks, not more than 500 or 1000 c.c. of gas being introduced at the beginning of the treatment. The gas is not allowed to flow in until free oscillation of the manometer indicates that the needle is in the interpleural space. The compression is maintained for from 1 to 2 years, and then the lung is allowed slowly to expand. The operation itself is not always successful and pleural effusion, gas embolism, pleural shock, and cardiac dilatation are among complications that may occur.

Medicinal Treatment.—Tuberculin is a useful adjuvant to other measures in certain cases, particularly those in which the general nutrition is good and the fever is slight. Contraindications are rapid emaciation, high temperature, active pleurisy, heart or kidney lesions, diabetes, and epilepsy. Hemoptysis

and intercurrent infections call for suspension of the injections for a time. No matter which tuberculin is selected, the initial dose should be small— $\frac{1}{10000}$ mg. of old tuberculin (O. T.) or tuberculin residue (T. R.). The injections should be given at first once or twice a week, the dose being gradually increased, but never large enough to cause a reaction, not even a slight rise of temperature. The maximum dose varies with the individual. With O. T. it may be as high as 1000 mg. or as low as a few hundredths of a milligram. Of T. R. the final dose may reach 10 mg. or more. If evidences of increasing sensitiveness appear, the injections should be stopped for a time and then resumed with smaller doses. As a rule, it is not advisable to administer tuberculin to ambulant patients unless their tuberculosis is of the more chronic or localized form.

Creosote is often useful when the expectoration is copious and purulent. The dose should be cautiously increased from 1 to 2 minims to 10 minims three times a day. Gastric irritation and nephritis are contraindications to its use. Creosote carbonate and guaiacol carbonate are free from the disagreeable odor and taste of creosote itself and appear to be equally efficacious. Arsenic, in small doses over a long period, is sometimes a valuable stimulant to nutrition. Iron is of service only when there is pronounced anemia. Nux vomica may often be given with advantage. Alcohol is not usually indicated, but sometimes in advanced cases whisky, brandy or champagne is of benefit in stimulating the appetite and lessening tissue waste. Calcium hypophosphite and other salts of calcium have been extensively employed as general tonics, but they are of doubtful value.

Treatment of Symptoms and Complications.—*Cough* that is effectual in removing accumulated secretions from the respiratory passages should be encouraged rather than checked. Morning cough, if accompanied by very viscid sputum, may be made easier by the administration of hot water containing a little sodium bicarbonate or aromatic spirits of ammonia. Expectorants in the form of syrups should be avoided. Ammonium chlorid, terpin hydrate, and the creosote derivatives may favorably influence both the cough and the expectoration when attacks of acute bronchitis supervene. Irritable, dry cough may often be controlled by discipline, the patient being trained to overcome the desire to cough by his own volition. Rest in bed and regulation of diet are valuable aids. In early cases the application of a small blister over the affected area frequently affords relief. Lozenges containing gelatin, Iceland moss, acacia, etc., with menthol are worthy of trial. Inhalations are often very effective. They may be given by means of a perforated metal inspirator, fitted over

the nose and mouth, containing a sponge upon which the volatile drug is placed. A mixture of equal parts of creosote, spirit of chloroform and alcohol is suitable for the purpose. The following is another useful combination:

℞. Spiritus chloroformi
 Creosoti
 Eucalyptol
 Olei pini sylvestris..... āā f 3ii (8.0 mls).—M.

Steam charged with creosote, compound tincture of benzoin or terebene is sometimes equally beneficial. The vapor may be inhaled from a paper cone fitted over the mouth of a pitcher containing boiling water and the drug. Intratracheal injections (1 per cent. of creosote or guaiacol or 2 per cent. of menthol in olive oil) may also be tried. Cough that depends upon inflammation of the pharynx or larynx calls for appropriate local treatment, and that due to acute pleurisy will usually yield to strapping of the chest or to counterirritation. Sooner or later in many cases it becomes necessary to employ internal sedatives. Of these the least objectionable are codein, heroin, spirit of chloroform and diluted hydrocyanic acid. Such combinations as the following are useful:

℞. Codeinæ sulphatis..... gr. iv-vi (0.25-0.4 gm.)
 Spiritus chloroformi..... f 3ii (8.0 mls)
 Glycerini
 Succī limonis..... āā f 3ss (15.0 mls)
 Aquæ..... q. s. ad f 3iii (90.0 mls).—M.

Sig.—A teaspoonful as occasion demands.

℞. Codeinæ sulphatis..... gr. iii (0.2 gm.)
 Acidi hydrocyanici diluti..... ℥. xxiv (1.5 mls)
 Glycerini..... f 3ss (15.0 mls)
 Aquæ..... q. s. ad f 3iii (90.0 mls).—M.

Sig.—Two teaspoonfuls from one to four times a day.

Night-sweats are controlled, as a rule, by rest, a constant supply of fresh air, and regulation of the digestive functions. If necessary, the patient may be bathed at night with cool water and alcohol, or with vinegar. An ice-bag applied to the abdomen for two or three hours in the evening is also useful. When the patient is very weak it may be advisable to give him at bedtime a glass of cold milk with brandy, and a small amount of some simple food once or twice during the night. Of drugs, the most reliable are atropin, $\frac{1}{200}$ – $\frac{1}{100}$ grain (0.0003–0.00065 gm.), picrotoxin, $\frac{1}{100}$ – $\frac{1}{60}$ grain (0.00065–0.001 gm.), agaric acid, $\frac{1}{6}$ – $\frac{1}{2}$ grain (0.01–0.03 gm.), and camphoric acid, 15 grains (1.0 gm.), in cachets or capsules.

Digestive Disturbances.—In many cases the first indication is to correct disordered digestion. No medicines that are likely to irritate the stomach should be ordered. Only the most bland and readily digestible food should be allowed. The time of eating, as well as the character of the nourishment, should be carefully revised. The various measures and drugs that are serviceable in uncomplicated digestive disturbances are applicable here. The most potent measures are fresh air and rest. Acute indigestion brought on by overeating is often promptly relieved by a mercurial purge followed by a saline. When anorexia and slow digestion are the chief features, an alkali with a vegetable bitter before meals often has a good effect. Such a combination as the following may be employed:

R̄. Sodii bicarbonatis..... ʒi (4.0 gm.)
 Tincturæ nucis vomicæ..... f ʒi (4.0 mls)
 Infusi gentianæ compositæ.. q. s. ad f ʒviii (240.0 mls).—M.
 Sig.—Tablespoonful before meals.

Vomiting that depends upon extreme irritability of the stomach sometimes yields to such sedatives as bismuth subnitrate, cerium oxalate, and hydrocyanic acid, taken before meals. Emesis that is excited by cough not rarely subsides when the patient is kept in bed and put on a liquid diet. Chloroform water taken a few minutes after the meals is useful. Counterirritation over the affected area in the lung is often of service. Vomiting that is caused by ulceration of the epiglottis or larynx will call for local anesthetics—cocain, orthoform, anesthesin.

Diarrhea.—Diarrhea, the result of indigestion, usually yields promptly to restriction of the diet, rest, and the administration of a mild mercurial. Persistent diarrhea will demand the use of bismuth subnitrate, 20 to 30 grains (1.3–2.0 gm.), combined with opium and intestinal antiseptics—salol, bismuth-betanaphthol, or creosote. Combinations of tannigen or tannalbin—3 to 10 grains (0.2–0.6 gm.)—with bismuth compounds are also useful.

R̄. Tannigen..... ʒss–ʒi (2.0–4.0 gm.)
 Bismuthi subcarbonatis..... ʒiii (12.0 gm.)
 Codeinæ sulphatis..... gr. iii (0.2 gm.).—M.
 Fiant chartulæ No. xii.
 Sig.—One powder three or four times a day.

Hemoptysis.—The treatment of hemoptysis is considered on page 656.

Insomnia.—The treatment of the insomnia coincides in many cases with that of the cough, the fever, and the night-sweats. Fresh air, rest, and regulation of the diet are valuable aids.

A glass of hot milk, malted milk or cocoa may be taken just before retiring. If the feet are cold a hot foot bath at night or the placing of hot bottles in the bed will often prove effective. Drugs should be used only after other measures have failed. The least objectionable sedatives are the bromids and barbital.

Fever.—In many cases the fever yields to rest in bed or in a reclining chair, combined with open-air treatment. When the temperature is high cold sponging is to be recommended. Antipyretic drugs are contraindicated. If the digestion remains good no change need be made in the diet on account of the pyrexia.

Pleurisy.—Mild attacks of pleuritic pain are best treated by sinapisms, applications of iodine, or strapping the affected side. If the pain is severe dry cups or small blisters may be used. Internally, the salicylates are sometimes of benefit. Occasionally, morphin is necessary. The treatment of pleuritic effusion in tuberculous patients is much the same as that of ordinary pleurisy with effusion. Thoracentesis, however, is not often advisable in the late stages of tuberculosis if the effusion is only moderate and does not seriously embarrass the cardiac or respiratory functions.

Pregnancy.—If the patient is seen prior to the fourth or fifth month and the tuberculosis is extensive or active the uterus should be emptied at the earliest possible date. After the fourth or fifth month an expectant plan of treatment is preferable.

SYPHILIS

The only certain means of prevention is avoidance of the sources of infection. As the disease is acquired in the large majority of cases through illicit coitus, continence is, of course, the chief safeguard. Accidental infection, however, is not infrequent, and therefore the patient should be told of the danger of transmitting the disease by kissing, by contaminating utensils that others are likely to use, etc. The prophylactic treatment suggested by Metchnikoff, which consists in rubbing a 33 per cent. calomel ointment into the penis and foreskin after infective contact, has been employed in armies and navies with considerable success. The use of the ointment before coitus still further lessens the danger of infection.

Fournier and Guenot, Lacapère and Laurent, Michel and Goodman report favorably on the abortion of syphilis by moderate doses of arsphenamin used during the primary incubation period. Marriage should be prohibited to a syphilitic person until at least 4 years after the date of infection, and even then if thorough treatment has not extended over 3 years or if

symptoms have been present within a year. If marriage should occur before the time specified and the wife conceive, she should undergo active treatment throughout the whole period of pregnancy.

As to public prophylaxis, instruction of the laity about syphilis itself and the menace to health of prostitution, the establishment of free dispensaries and provision in all general hospitals for the treatment of venereal diseases are the most hopeful means of controlling the spread of the disease. State regulation of prostitution has proved ineffectual.

For the **local treatment** of the primary sore reference must be made to surgical works. The experiments of Neisser upon apes and of Brown and Pearce upon rabbits demonstrate the futility of excision. These observers found that there is no appreciable time during which the infection can be regarded as confined to the portal of entry.

Constitutional treatment should be begun as soon as the diagnosis is certain, the dark-field microscope being employed for the detection of the spirochetes in all suspicious lesions. The three potent internal remedies are arsphenamin and its allies, mercury and iodine, preferably in the form of potassium iodide. Of these remedies, probably only the first two have spirochæticidal action. *Arsphenamin* suppresses the manifestations of syphilis more rapidly than any other drug, and there is little doubt that many patients are cured by repeated doses, especially when it is used early and is alternated with mercury. The intravenous method of administration is now employed almost exclusively, and as there is considerable danger of phlebitis and of sloughing of the tissues under certain conditions, only persons who have been properly instructed in the procedure should attempt it.

The dose of arsphenamin and the frequency of its administration vary with the stage of the disease, the general health of the patient, the age, and the sex. For robust men with active syphilis the maximum dose is 10 grains (0.6 gm.). For less vigorous men and for women the dose should be from 4 to 8 grains (0.25–0.5 gm.), and for children, 2 to 5 grains (0.13–0.3 gm.). Neoarsphenamin has advantages over arsphenamin in being readily soluble in water and of neutral reaction, but, it seems to be somewhat less effective than the older preparation. The maximum dose is 15 grains (0.9 gm.). Arsphenamin should be given with at least 120 mls of saline solution for each 10 grains (0.6 gm.) and introduced into the vein, preferably one at the elbow, from a gravity buret (for the method of preparing the solution see p. 322). The solution should be used at once after

it is made. Not less than 5 minutes should be allowed for the 120 mils to enter the vein. The patient should be recumbent during the treatment and should remain so for several hours after it.

Solutions of *neoarsphenamin* may be administered from a buret by the gravity method or directly from a Luer syringe. For intravenous injection the drug should be dissolved, with but slight agitation, in from 50 to 20 mils of freshly distilled, warm (75° F.), sterilized water. Unless the solution is brilliantly clear it should be rejected, as cloudy solutions invariably cause severe reactions. For intramuscular injections a Luer syringe should be used with needles 1½ to 2 inches long. The injections are best made into the buttocks. About 3 mils of freshly distilled water should be used for each 2½ grains (0.15 gr.) of neoarsphenamin.

As a rule, arsphenamin or neoarsphenamin is best given every few days or a week for 5 or 6 injections, the intervals being used for the administration of mercury. Between each course of the drug a rest period of 6 weeks is usually advised. In primary syphilis at least two courses with six months of mercurial treatment should be given even if the Wassermann reaction is negative. In secondary syphilis it is often necessary to give 3 or 4 courses of arsphenamin with mercury before the serum reactions become negative. Some syphilographers advocate a short course of mercury before the injections of arsphenamin in florid syphilis, hoping in this way to avoid the intensification of the rash that sometimes follows arsenical treatment. In tertiary syphilis it is advisable to combine the courses of arsphenamin with the prolonged use of both mercury and potassium iodid. Indeed, in tertiary lesions of the viscera and bones, as well as in latent syphilis with a positive Wassermann reaction, better results are not rarely secured from the prolonged use of mercury and potassium iodid than from arsphenamin alone. In all cases prolonged medical supervision is necessary, for it is only when the clinical and serologic findings are constantly negative, on repeated examinations for many years, that we can regard the cure as probable. An isolated negative Wassermann reaction, especially in the absence of a provocative injection of arsphenamin, is no criterion that the infection is extinct. With persistent positive serologic findings a course of treatment should be given annually or biannually.

The intraspinal use of arsphenaminized serum, as elaborated by Swift and Ellis, is a distinct advance in the treatment of syphilis of the central nervous system, especially gummatous infiltrations, and to a less extent tabes and general paresis. The technique is briefly as follows: An hour after an intravenous injection of arsphenamin or neoarsphenamin, 60 mils of blood are withdrawn

by venepuncture. The serum of this blood, after being diluted with normal saline solution to form a 40 per cent. mixture, is kept at a temperature of 56° C. for one-half hour. Later in the day a lumbar puncture is made and an amount of fluid equivalent to the amount to be introduced is withdrawn. While the needle is still in place 30 or 35 mls of the diluted serum are allowed to flow into the subarachnoid space by gravity through a rubber tube (40 cm. in length) connected to the barrel of a Luer syringe. After the treatment the patient should be kept in bed with his feet slightly elevated for twenty-four hours. Untoward symptoms, such as headache, pains in the legs and vesical disturbances are sometimes noted. The treatment is repeated at intervals of from 10 days to 2 weeks and for 4 to 6 administrations according to the patient's tolerance. In some cases better results are secured by omitting the preliminary intravenous injection and using serum which has been heated and to which has been added directly the arsphenamin. The primary dose of the latter should not exceed $\frac{1}{4}$ milligram (Ogilvie's method).

Mercury may be given in syphilis by the mouth, by inunctions or by intramuscular injections. By the mouth, the favorite preparations are the protoidid ($\frac{1}{4}$ gr.—0.015 gm.), the biniodid ($\frac{1}{16}$ gr.—0.004 gm.) and for children, mercury with chalk (1 gr.—0.06 gm.). Whatever preparation is selected or whatever method of administration is employed, the dose should be the maximum the patient can tolerate and the treatment should be given in course of 5 or 6 weeks duration, with intermissions of from 1 to 3 months, for 2 years or longer, according to the clinical and serologic findings. During the administration of the mercury the teeth should be brushed after each meal and the mouth should be cleansed several times a day with a mild antiseptic wash.

Inunction is an effective method of administering mercury and has the advantage of not disturbing the digestion. The disadvantages of the method are the publicity that it entails, its unpleasantness, and the uncertainty of the dosage. It is carried out by rubbing 30 grains (2.0 gm.) of fresh mercurial ointment thoroughly into the skin every day for six consecutive days, a different area being selected for each inunction, so as to avoid irritation. On the seventh day a warm cleansing bath is substituted for the rubbing. Favorite sites are the inner sides of the arms and thighs, the groins, the chest and the abdomen. The treatment should be continued for 5 or 6 weeks and then omitted for from 1 to 3 months.

Intramuscular injections of mercury yield excellent results. They permit of more exact dosage and more close supervision of the patient than oral administration or inunction. On the other

hand, they are more or less painful and occasionally result in serious toxic symptoms, especially if insoluble preparations are used. Soluble salts act more promptly but cause more pain. A freshly made 1 per cent. solution of mercuric benzoate in distilled water, with the addition of 2.5 per cent. of sodium chlorid, may be injected daily in doses of 30 to 45 minims (2.0–3.0 mls) with comparatively little pain. The injections should be made into the gluteal muscles every day or every other day in courses lasting from 4 to 6 weeks, and then discontinued for about 6 weeks. One of the best of the insoluble preparations, if carefully compounded, is gray oil, a 40 per cent. suspension of metallic mercury in oil. Of this 5 minims (0.3 ml) may be given once a week for a period of from eight to twelve weeks. Schamberg has found the following combination very efficient and relatively free from pain:

℞. Mercury (bi-distilled)..... gr. cccx (24.0 gm.)
 Lanolin..... gr. cccx (24.0 gm.)
 Cocain oleate..... gr. xv (1.0 gm.)
 Creosote..... f ʒii (8.0 mls)
 Liquid petrolatum..... ꝑev (7.0 mls).—M.

0.3 ml = 0.2 gm. of mercury

5 minims = about 3 gr. of mercury.

The usual dose is about 3 minims (0.2 ml) every 7 days for a series of 10 injections, which constitutes a course.

The *iodids* have no spirochæticidal action, nevertheless as adjuvants to arsphenamin and mercury they are invaluable, especially in tertiary and latent cases and those involving the nervous system. It has been suggested that their resorptive action on syphilitic deposits favors the access of arsenic and mercury to the spirochætæ. Although moderate doses are sometimes sufficient it is generally advisable to increase the amount gradually until 2 or even 3 drams (8.0–12.0 gm.) are being taken daily. Milk is the best vehicle. In some cases an iodid may be advantageously combined with mercury, as in the following formula:

℞. Hydrargyri chloridi corrosivi..... gr. i (0.065 gm.)
 Potassii iodidi..... ʒiii–ʒi (12.0–30.0 gm.)
 Syrupi sarsaparillæ compositi..... f ʒii (60.0 mls)
 Aquæ..... q. s. ad f ʒiv (120.0 mls)

Sig.—Two teaspoonfuls in water three times a day after meals.

Iodids have no place in the treatment of the early manifestations of syphilis.

Aside from specific medication, general hygienic measures are of the utmost importance. The use of alcohol should be interdicted and the patient should be warned against excesses of all kinds.

In some cases, especially if the nervous system is involved, complete rest, at least for a time, is imperative. When there is cachexia much benefit accrues from the use of iron and bitter tonics.

Syphilitic infants until they are a year old are best treated by mercurial inunctions or the administration of mercury with chalk. The inunctions are usually made over the abdomen, mercurial ointment of one-fourth to one-half strength being employed for the purpose. If the infant is nursing, the mother should at the same time be given intravenous injections of neoarsphenamin. After the first year neoarsphenamin may be given intravenously to infants in doses of 50 to 75 mg. for each 10 pounds of body-weight.

SCARLET FEVER

The treatment of scarlet fever is virtually symptomatic, for while a number of favorable reports on the use of *blood-serum* of patients convalescing from the disease have recently appeared (Landsteiner, Levaditi, Zingher, Weaver, Kling and Widfelt), the value of this remedy has not been fully demonstrated. From 30 to 90 mls of the serum are given intramuscularly, and repeated if necessary.

Rest in bed from the onset is imperative and should be continued for at least three weeks, even in the mildest cases. Milk, junket, koumiss, ice cream, gruels, toasted bread, and fruit-juices are suitable forms of nourishment. So as not to tax unnecessarily the kidneys, animal broths, with the exception of oyster or clam broth, should be withheld until convalescence is well established. Water should be given freely to relieve thirst and to keep the secretions active. The addition of an alkaline diuretic, such as potassium citrate, to the water serves a useful purpose. The bowels should be kept regular by mild saline aperients or cascara sagrada. Irrigation of the throat with normal salt solution or a 4 per cent. solution of boric acid is usually advisable if the *angina* is severe, but if the procedure meets with serious resistance it is better to dispense with it. In older children mild antiseptic gargles may be employed with advantage.

In many cases no special medication is required. Sponging with tepid water once or twice a day has a soothing effect. If the *vomiting* is severe it may be necessary to withhold food for a time and to administer cracked ice, bismuth subcarbonate, or cerium oxalate. *High temperature* (above 103.5° F.) is best controlled by cold sponge baths, cold packs, or graduated tub-baths

(90° F. gradually reduced to 75° or 70° F.). In some cases with high fever and extreme restlessness immersion for ten minutes in water at 105° F. reduces the temperature and exerts a pronounced sedative effect. Antipyretic drugs should, as a rule, be avoided. Daily inunctions of the body with cold cream, cocoa butter, or carbolized oil serve to allay *itching*. When *restlessness*, *insomnia* and *delirium* are not relieved by cold applications to the head and the hydrotherapeutic measures already suggested, the use of chloral is advisable. From 2 to 3 grains (0.13–0.2 gm.) for a child of 2 to 4 years may be given in syrup of orange and water and repeated in two hours, if necessary. Sometimes a combination of a bromid and chloral acts better than the latter alone. A few small doses of acetphenetidin (2 grains,—0.13 gm.) may also prove efficacious.

Adenitis is best treated by applying an ice-bag or cold compresses. An ointment of ichthyol (20 per cent.) has been recommended. When suppuration occurs the abscess should be opened and treated according to modern surgical practice.

Otitis should be sought for at frequent intervals, as in young children, especially, its occurrence is not always suggested by pain. In the cases in which earache develops, dry heat to the ear is sometimes effective. Not rarely, however, it may be necessary to irrigate the ear with hot water and then to drop into it a solution of cocain (4 per cent.). Bulging of the tympanic membrane calls for incision and liberation of the pent-up pus.

Arthritis may be treated by wrapping the affected joints in cotton-wool, after first painting them with tincture of iodine, and by administering acetylsalicylic acid. *Circulatory weakness* will require use of such drugs as digitalis, caffeine, camphor, etc.

Should *nephritis* develop, cupping (dry or wet) over the loins, followed by hot fomentations or poultices, often proves useful. Aperients, especially salines, are indicated. Warm baths, hot-packs or hot air baths should be used to promote diaphoresis, and alkaline diuretics (potassium citrate, potassium acetate, potassium bicarbonate) should be given to increase the urinary output.

SMALLPOX

Absolute rest in bed, light bed-clothing, an easily assimilable diet, and the free use of water are requisites of treatment. The sick-room should be well ventilated, screened, and kept at a temperature of 65°–68° F. In the invasive stage milk and light broths are suitable forms of nourishment. Orangeade, lemonade,

etc., are usually well received, and, in addition to supplying an abundance of water, increase slightly the caloric value of the diet. During the stage of suppuration, the most exhausting period of the disease, the diet should be as nutritious as the patient can tolerate. Unfortunately, the soreness of the throat and mouth makes the ingestion of sufficient nourishment difficult. As a rule, however, milk, well-cooked farinaceous foods, and gelatin preparations can be introduced in addition to milk. When there are symptoms indicative of exhaustion, alcohol in the form of brandy or whiskey, may often be used with advantage. It adds calories to the diet, stimulates digestion, and promotes sleep. Quinin, in small doses, is also of service in the adynamia of sepsis. Stimulants (digitalis, caffeine, strychnin, camphor) are called for in the event of *circulatory failure*.

The severe *lumbar pains* will require the application of hot-water bags and the administration of morphin hypodermically, or of acetphenetidin in moderate doses by the mouth. Sinapisms should not be used, as the pocks always appear in great profusion upon irritated surfaces. *Gastric irritability* may usually be controlled by the use of cracked ice, champagne, bismuth subcarbonate, cerium oxalate or cocain. *Restlessness, jactitation, and insomnia* will require the use of morphin, bromids or chloral. Patients who are actively delirious or who are the subjects of delusions must be carefully watched and, if necessary, strapped in bed with folded sheets, since they not rarely attempt to escape through the window or even to commit acts of violence. The fever of the initial stage is best controlled by sponging the body with cold water and applying an ice-bag to the head. The fever of the suppurative stage may be kept within bounds by cool or tepid packs. Cold baths are not, as a rule, well borne. An attempt should be made to keep the *nasopharynx* clean. For this purpose Dobell's solution, diluted with 2 or 3 parts of water, or boric acid solution (2 per cent.) may be used as an irrigation or spray, or applied by gentle swabbings. If the secretions are very offensive a solution of potassium permanganate (1 : 4000) may be substituted.

The eyes should also be kept clean by frequent applications of warm boric acid solution—10 grains to the ounce (0.65 gm.—30.0 mils.). In purulent conjunctivitis a few drops of argyrol (10–20 per cent.) may be dropped into the conjunctival sac once or twice a day. If keratitis supervenes, atropin should also be used to allay inflammation, produce mydriasis and prevent iritis, and the eyes protected with cold or warm compresses. *Dysphagia* is often benefited by pellets of ice, demulcent drinks, sprays of cocain (2 per cent.) or lozenges of orthoform (1 gr.—0.06 gm.).

When *laryngeal symptoms* are threatening, the use of the steam tent and of inhalations of medicated steam (compound tincture of benzoin, eucalyptol, etc.) are often of great benefit. If edema of the larynx supervenes it may be necessary to scarify the affected tissue or to perform tracheotomy.

The Eruption.—The application of cold compresses is, perhaps, the best means of allaying burning and itching. Compresses wet with a cold solution of boric acid (3 per cent.) may be kept constantly on the face, hands and forearms. Ointments containing phenol (3 per cent.) are also effective. Many remedies have been recommended to prevent pitting, but it is doubtful whether any is really efficacious. An old plan was to open the vesicles and touch their bases lightly with a stick of silver nitrate. Dujardin-Beaumetz recommended very highly an ointment of sodium salicylate (4 parts) and cold cream (100 parts). Hebra found continuous warm baths of value. Schamberg claims good results from applications to the face, once or twice a day, of tincture of iodine, undiluted, or, if the skin is especially sensitive, diluted one-half. Finsen, Feilberg and others have advocated the exclusion of the chemical rays of light from the sick-room, red light only being admitted, but this plan of treatment has not been found particularly efficacious by those who have adopted it and has the drawback of putting a check on the supply of fresh air. In the stage of desiccation warm alkaline baths followed by inunctions with cold cream or olive oil are useful in allaying itching and in hastening the removal of the crusts.

Quarantine should be continued until decrustation is completed. After all the crusts are detached the patient should be given a bath of corrosive sublimate solution (1 : 10,000) and then a soap-and-water bath and a thorough shampoo. Finally, he should be removed to another room and given entirely clean under clothing.

MEASLES AND RUBELLA

The sick-room should be well ventilated, but free from drafts, and kept at a temperature of about 70° F. Even in the absence of complications, it is advisable for the patient to remain in bed for at least 10 days from the onset. On account of the photophobia, bright light should be excluded from the room or the bed so placed that the patient's face will be directed away from the windows. Cough is lessened by keeping the atmosphere of the room somewhat moist. The diet should be light. In the case of infants, the milk-mixture must be considerably diluted. For older children and adults—milk, junket, light broths, soft

boiled eggs, and corn starch preparations are suitable forms of nourishment. Water should be proffered at frequent intervals. The fever is seldom sufficiently high to demand bathing, but a tepid sponge bath once a day is requisite. Hot baths and hot drinks are indicated when the rash is delayed. If there is much itching, cold cream or olive oil may be applied to the skin after it has been bathed and dried.

Constipation is best relieved by enemias or glycerin suppositories. Irritation of the eyes is benefited by frequent applications of a 3 per cent. solution of boric acid. When the conjunctivitis is severe the eyes should be protected by dark glasses.

Cough is the symptom that most frequently requires attention. Such a mixture as the following is often useful:

R.	Potassii citratis.....	℥ii (8.0 gm.)
	Tincturæ opii camphoratæ.....	f℥ii-iv (8.0-15.0 mls)
	Tincturæ belladonnæ.....	℥xxl (2.5 mls)
	Glycerini.....	f℥ii (8.0 mls)
	Aquæ.....	q. s. ad f℥iii (90.0 mls).—M.

Sig.—A teaspoonful every two or three hours for a child of four years.

When the bronchitis is severe, mild sinapisms may be applied to the chest with advantage. Diarrhea usually yields to bismuth subcarbonate, with or without opium. Pronounced nervous symptoms are best treated by warm tub-baths and the administration of appropriate doses of a bromid. The ears should be examined frequently, even in the absence of earache. When pus is detected, it should be evacuated at once by free incision of the tympanic membrane.

During convalescence tonics—iron, strychnin, arsenic and cod-liver oil—are frequently indicated.

MUMPS

(Epidemic Parotitis)

The patient should be confined to bed and, as mastication is painful, given a diet of soft, bland food. A mild aperient may be administered at the beginning of the attack. In mild cases protection of the affected glands with cotton batting will be sufficient local treatment. If the pain is severe several thicknesses of gauze wrung out of a saturated solution of magnesium sulphate may be applied and covered with oiled muslin, or an ointment of guaiacol (5-10 per cent.) or of ichthyol (10-20 per cent.) may be used. Small doses of acetphenetidin or of codein may be necessary.

Orchitis is best treated by elevating the testicle and applying an ointment of guaiacol (10-20 per cent.) or of ichthyol (20 per

cent.). Strapping is inadvisable. Applications to either the parotid gland or testicle should be made without friction or massage.

WHOOPIING COUGH

(Pertussis)

An abundance of fresh air and sunlight, protection from changes of weather, and a light but nutritious diet are important elements of treatment. During the catarrhal stage it may be advisable to keep the patient in his room or even in bed, but later, if the weather is favorable, he need not be confined indoors. A change of air, especially to the seashore, is often a valuable aid in protracted cases. If vomiting is very frequent, it is important to give small feedings, preferably of liquids, immediately after the paroxysms. Occasionally it may be necessary to use predigested foods or to have recourse to nutritive enemata.

The drugs of most value in lessening the severity and frequency of the paroxysms are belladonna, antipyrin and bromids. Belladonna to be effective must be given in doses sufficient to produce flushing of the cheeks and dilatation of the pupils. To a child of 2 years 2 minims (0.12 mil) of the tincture may be given three or four times a day, and the dose gradually increased until the physiologic effects of the drug are evident. The dose being taken when the limits of toleration are reached should be maintained for a considerable period. Antipyrin, in doses of 2 to 3 grains (0.13–0.2 gm.) every three or four hours for a child of 2 years, is sometimes very efficacious. Bromid of sodium or potassium, in doses of 5 grains (0.3 gm.) three times a day, for a child of two years, is also useful. It may often be combined advantageously with antipyrin or belladonna, as in the following formula:

R. Sodii bromidi..... ʒi (4.0 gm.)
 Antipyrinæ..... gr. xxx (2.0 gm.)
 Glycerini..... f ʒi (4.0 mls)
 Aquæ menthæ piperitæ.... q. s. ad f ʒiii (90.0 mls).—M.

Sig.—A teaspoonful in water three or four times a day for a child of 3 years.

Benzyl benzoate sometimes affords relief, but it often fails. Ten to fifteen minims (0.6–1.0 mil) of a 20 per cent. emulsion may be given in milk or sweetened water four times a day.

Vaccines of the Bordet-Gengou bacillus have been used to a greater or less extent, but their curative value is somewhat doubtful. However, as they are apparently harmless they may be tried in severe cases. Four injections may be given with one

day intervening between each. The first dose being 1 billion, the second 2 billion, the third 4 billion and the fourth 6 billion.

Chloral or codein are sometimes required at night to produce sleep. If the seizures are very violent, chloroform (a few drops on a handkerchief) may be given by inhalation. The inhalation of volatile antiseptics is of undoubted service in some instances. For this purpose compound tincture of benzoin, creosote, or eucalyptol may be vaporized in a croup kettle or inhaled from a respirator worn over the nose and mouth. For the relief of vomiting, the application of an elastic abdominal belt has a well-deserved reputation. The belt recommended by Kilmer is made of linen, with a strip of elastic webbing, two inches wide, inserted on each side. It extends from the axillæ to the pubes and laces in the back.

During convalescence tonics—iron, quinin, strychnin, and cod-liver oil—are frequently required.

ACUTE RHEUMATISM

Absolute rest in bed is essential and should be maintained, even in the absence of cardiac involvement, for at least ten days after the arthritic symptoms have completely subsided and the temperature has become normal. To guard against chilling of the body, the patient should wear a loose flannel night dress and, if the weather is cool, lie between blankets. The room should be well ventilated, but free from drafts. Milk, cereals, bread and butter, eggs and light broths are suitable forms of nourishment during the febrile period. After the temperature has become normal a liberal diet, including meat, is advantageous. The free use of water and lemonade should be encouraged. The bowels should be regularly moved by mild laxatives, preferably salines. When sweating is profuse the patient is made more comfortable by drying the skin with a soft absorbent towel and then sponging it lightly with alcohol. Spraying or swabbing the throat with alkaline antiseptic solutions is desirable, but even when the tonsils are seriously affected, tonsillectomy during the course of the infection is inadvisable, unless the attack is unduly prolonged and refractory to treatment.

Internal Medication.—Salicylates have power to control the symptoms, but they apparently do not lessen the tendency to endocarditis. Usually about 20 grains (1.3 gm.) of sodium salicylate should be given every three hours until the pain is definitely relieved and the fever is reduced or until ringing in the ears or other untoward symptoms indicate that the limit of tolerance has been reached. Even in children from 8 to 10 years of age a

dose of at least 10 grains (0.6 gm.) every three hours is advisable. The possibility of large doses causing delirium, even maniacal excitement, in susceptible persons should be borne in mind. As the pain and fever lessen, the size of the dose or the frequency of administration should be reduced, but the treatment should not be discontinued until at least a week after the disappearance of the symptoms. Alkalis, such as potassium bicarbonate, potassium citrate, or sodium citrate, are also of service, for while they probably exert no influence on the rheumatism itself, they lessen the tendency of the salicylates to irritate the stomach. The dose of the alkali should be about equal to that of the salicylate, and the two drugs may be given in combination, as in the following prescription:

R. Sodii salicylatis
 Potassii bicarbonatis..... āā ʒiv (15.5 gm.)
 Aquæ menthæ piperitæ..... fʒvi. (180.0 mls)—M.
 Sig.—A tablespoonful in water every three hours.

Generally speaking, sodium salicylate is the most efficacious of the salicylates and should be tried first, as a rule, in all severe forms of the disease. However, in mild attacks, or in cases in which sodium salicylate is not well borne or fails to do good, one of the esters, especially acetylsalicylic acid (aspirin) may be substituted. Salicylic acid itself is too irritant for internal use and phenyl salicylate (salol) is more poisonous and much less reliable than the sodium salt or the acetyl ester. When no salicylic compound can be tolerated by the mouth, sodium salicylate may be administered by the rectum. For an adult 2 drams (8.0 gm.) in 150 mls of thin starch water may be injected well up into the bowel after the use of a cleansing soap-sud enema, and repeated every 12 or 24 hours. Conner has administered sodium salicylate intravenously with good results. He gives 15 to 30 grains (1.0–2.0 gm.) every 8 to 12 hours, using a fine needle to avoid thrombosis.

Morphin is sometimes required to relieve intense pain, subdue restlessness and procure sleep. Acetphenetidin, antipyrin, and phenylcinchoninic acid (atophan), in moderate doses (5 gr.—0.3 gm.), are also useful adjuvants to salicylic compounds when the pain is very severe. When adynamia is marked quinin, as recommended by Garrod, Duckworth and Da Costa, may prove beneficial. Anemic patients are usually benefited by iron. Indeed, when the ordinary remedies fail, syrup of iodid of iron, in large doses (1–3 dr.—4.0–12.0 gm. daily), as recommended by J. C. Wilson, is sometimes effectual. Vaccines, even when prepared from the patient's own bacteria, usually fail. Daily intravenous

injections of a foreign protein, such as stock typhoid vaccine, are sometimes successful, however, in refractory cases, although they not rarely cause severe reactions.

Cerebral rheumatism is best treated by cold sponging or cold baths. Moderate venesection and lumbar puncture are worthy of trial. The treatment of endocarditis and of pericarditis is considered on pages 670 and 672 respectively. The importance of prolonged, absolute rest in all cases in which the heart becomes affected cannot be overestimated. The patient should not be permitted to leave his bed for several weeks after the fever has subsided, or if tachycardia or arrhythmia is present, until this has entirely disappeared, and even then the amount of his exertion should be carefully graduated, the effect on the pulse of each additional effort being used as a guide.

Local Treatment.—In mild cases the application of cotton-batting or lamb's wool to the affected joints will suffice. When the pain is severe compresses soaked in a saturated solution of magnesium sulphate and covered with oiled muslin often afford relief, but, as a rule, applications of methyl salicylate, diluted with 1 or 2 parts of cotton-seed oil, are more effective. A mixture of equal parts of guaiacol and glycerin is also useful. In some cases counterirritation by means of a fly blister 2 inches square on each side of the joint yields better results than any other form of local treatment. No matter what application is made, it is important that the inflamed joints should be kept at complete rest in a position of relaxation or moderate flexion. This may be accomplished by means of small sand bags or of padded splints and a roller bandage.

Lingering swelling often yields to an ointment of mercury, belladonna and salicylic acid with firm strapping of the articulation. The following ointment may be used.

R̄.	Acidi salicylici.....	℥iss (6.0 gm.)
	Unguenti belladonnæ	
	Unguenti hydrargyri.....	āā ℥ss (15.0 gm.)
	Adipis.....	℥iv (125.0 gm.)

In other cases venous hyperemia by Bier's method will be found efficacious. The bandage should be applied for about two hours, twice a day. It should be tight enough to cause redness but not edema. Baking with superheated air and gentle manipulation and massage are useful in overcoming persistent stiffness.

Convalescence must be carefully guarded. The patient should be warmly clothed, well fed, given iron and other tonics, and, if necessary and feasible, removed for a time to a more salubrious environment.

ACUTE POLIOMYELITIS

During the acute stage the treatment should be that of other acute infections. Absolute rest in bed for several weeks, even in the mildest cases, is essential. Counterirritation interferes with rest and can do no good. Mild diaphoretics and hot packs or hot baths (100° F.) for fifteen minutes, twice a day seem to be of benefit. Hexamethylamin (20–30 gr.—1.3–2.0 gm.—daily) has been recommended, but as it yields virtually no formaldehyd in the cerebrospinal fluid, it is of doubtful value.

Intraspinal and intravenous injections of the serum of convalescent patients has been tried by Netter, Amoss and Chesney, and others, but up to the present time the results have not been conclusive. Rosenow reports good results from intravenous and intramuscular injections of an immune horse serum prepared by repeated inoculations with a pleomorphic streptococcus isolated from the central nervous system in human poliomyelitis. Of 121 patients treated in the early stages, none died and but one showed slight residual paralysis. Severe pain in poliomyelitis will require the use of acetylsalicylic acid, acetphenetidin, or morphin. Lumbar puncture usually affords much relief. In the event of respiratory failure, oxygen inhalations and artificial respiration should be tried.

The affected limbs should be wrapped in cotton-wool and maintained in such a position that the paralyzed muscles will not become overstretched or their antagonists overactive. After the lapse of three or four weeks mechanical treatment should be instituted and systematically practised for a year or a year and a half, if necessary. Massage and passive movements are especially useful in promoting the circulation in the paralyzed members and in counteracting the tendency to contractures. Electricity may also be used with advantage in many cases. The faradic current should first be tried and if to this there is no response recourse should be had to galvanism, the cathode being chosen as the active pole. The weakest current that causes contractions should be used and the applications should be made for ten minutes, four or five times a week. It is doubtful whether any good can be accomplished by using electricity unless the current produces muscular contractions. In the case of young children electric treatment should always be instituted very gradually, otherwise the application may cause so much alarm as to be distinctly harmful; and again, if contractions can be produced only by currents which cause pain it is better to dispense with electricity entirely and depend upon the other measures.

In the course of a few weeks, if the paralysis shows a tendency to recede, the patient should be encouraged to make voluntary

movements of the affected limbs, the amount of exercise being gradually increased as the power returns. Under no circumstances, however, should attempts at walking without assistance be permitted until the legs are strong enough to bear the weight of the body. Even when the paralyzed muscles show no further tendency toward recovery, much good may be accomplished by the application in suitable cases of light, well-fitting braces, or, if there is excessive contraction of healthy muscles, by tenotomies. In other instances nerve anastomosis, tendon transplantation, tendon-lengthening, or the resection of a joint may serve to increase the usefulness of an affected member.

EPIDEMIC ENCEPHALITIS

Treatment is largely empiric. Rest in bed, protection from excitement, an abundance of liquid and semi-liquid food, regulation of the bowels, and careful nursing are first in importance. Lumbar puncture with the removal of from 10 to 20 mls of spinal fluid, at intervals of 3 or 4 days, has been of service in some cases. Hexamethylenamin, in doses of 10 grains (0.6 gm.), three times a day, has been recommended, but it is of doubtful value. In cases with severe headache, restlessness, and insomnia bromids may be used with advantage. Marked muscular excitation is sometimes favorably influenced by phenobarbital in doses of $\frac{1}{2}$ to 2 grains (0.03–0.13 gm.), two or three times a day or scopolamin hydrobromid (hyoscin hydrobromid) in doses of $\frac{1}{150}$ of a grain (0.0004 gm.). During convalescence rest should be continued and supplemented by hydrotherapy and massage.

MALARIA

Quinin is the only reliable remedy for malaria. Methylene blue (3–5 gr. with half its weight of powdered nutmeg) is of some value, but it is decidedly less effective than quinin and should be employed only when there is some serious idiosyncrasy to the latter. As the youngest forms of the malarial parasites are more readily killed by quinin than the full-grown organisms within the red cells, it is usually advisable in tertian and quartan infections to give a single large dose of the drug (15 gr.–1.0 gm.) toward the close of paroxysm, that is when the temperature is beginning to fall. However, if the patient is seen some time after a chill, and another is not expected for thirty-six hours or more, it is better to begin the treatment at once and to give a

smaller dose of quinin (10 gr.—0.65 gm.) three times a day. The remedy should be continued in such amounts until the paroxysms cease and then given in the dose of (10 gr.—0.65 gm.) once a day for at least two months. The administration of calomel as a preliminary measure increases the efficacy of quinin, probably by facilitating its absorption. Under ordinary circumstances quinin should be given by the mouth. It may be prescribed in soft capsules, in cachets or in solution. The sulphate is probably as effective as any other preparation, although it is less soluble than the bisulphate and the dihydrochlorid. To children the drug may be given suspended in syrup of yerba santa or syrup of chocolate. During convalescence arsenic and iron may be given advantageously with quinin.

In estivo-autumnal infections larger doses of quinin are usually required than in tertian or quartan malaria, although it is rarely necessary to give more than 15 grains (1.0 gm.) three times a day. In pernicious malaria quinin should be administered intramuscularly (1 gram of the dihydrochlorid or of quinin-urca hydrochlorid in 10 mils of water, in the gluteal region, repeated once or twice) or, preferably, intravenously, 0.65 gram of the dihydrochlorid in 200 mils of salt solution, being cautiously introduced according to the arsphenamin technique (see p. 322).

As to the advisability of using quinin in blackwater fever there is much diversity of opinion, but the weight of authority seems to be in favor of withholding the drug during a paroxysm of hemoglobinuria unless there are numerous parasites in the blood. The intravenous method of administration, dissolving the quinin in large quantities of salt solution (300 mils) is preferred.

General Measures.—In acute malaria rest in bed and an easily digestible diet are requisites of treatment. During the cold stage of a paroxysm the patient should be well covered with blankets and given hot drinks. Morphine, $\frac{1}{6}$ grain (0.01 gm.) hypodermically, is often useful in mitigating the discomfort.

In the hot stage of a paroxysm much relief is afforded by sponging the body with cool water, giving cool drinks, and administering a moderate dose of acetphenetidin or acetanilid. Persistent vomiting is best controlled by the application of a sinapism to the epigastrium and the use of such sedatives as bismuth subcarbonate, cerium oxalate, iced champagne, etc.

In the treatment of persons with latent malaria (malarial carriers) Bass recommends 10 grains (0.65 gm.) of quinin sulphate every night for a period of eight weeks, or, in the event of a relapse, for longer periods. In malarial cachexia arsenic and iron are useful adjuvants to quinin. However, in many cases no decided improvements can be affected until a change of climate

is secured. Splenectomy has been performed in a number of cases with gratifying results, although the mortality in this condition is relatively high (Jonnesco, Mourdas, Finkelstein, Mayo).

AMEBIASIS

(Amebic Dysentery)

The treatment of acute cases and of all exacerbations is in general that of acute colitis from other causes, the important measures being absolute rest in bed; a diet of milk and lime-water, whites of eggs, beef-juice, milk toast, and custard; mild counter-irritation by means of mustard plasters or turpentine stupes; and the administration of a saline purge, castor oil or calomel to clear the bowels; and of some sedative, such as opium by the mouth or morphin hypodermically. Bismuth subcarbonate in large doses is also useful. When the rectum is very irritable ice suppositories, or injections of warm mucilage of starch (1 ounce—30.0 mls) or of cocain solution (10 min.—0.6 mil— of a 4 per cent. solution) may be employed with advantage.

After the subsidence of acute symptoms and in all other cases the restrictions on exercise and eating need not be so severe; however, quiet living, with many hours allotted to rest, and a diet of bland easily digestible food are imperative. Ipecacuanha in large doses has long been used as a special remedy, but it is only since 1912, when Rogers employed the alkaloid emetin subcutaneously, that the value of the drug has been definitely established. It is now generally believed that emetin is a true specific, destroying the amebæ in the tissues, and that its action is comparable to the specific tropism of quinin in malaria and of arsphenamin in syphilis. It may even prevent the formation of an abscess if given early in amebic hepatitis. To secure the best results $\frac{1}{2}$ grain (0.03 gm.) of emetin hydrochlorid should be given hypodermically twice a day, or 1 grain (0.065 gm.) once a day, for ten days or two weeks. If colic or severe diarrhea supervenes it may be checked by opium and bismuth subcarbonate. Even in the absence of severe diarrhea, large doses of bismuth subcarbonate (3 i—4.0 gm.), several times a day, may be given advantageously in conjunction with the emetin. Once in four or five days the bowels should be cleansed by a saline purge, and during the treatment the patient should remain in bed. After the disappearance of all symptoms, a stool obtained by the use of a saline cathartic should be examined once a month for several months and if amebæ are found the treatment should be repeated. Some observers have found that relapse is less likely to occur if

ipecacuanha, 30 to 60 grains (2.0–4.0 gm.), in salol-coated pills, is given daily for several days after the discontinuance of the emetin. To prevent vomiting, the drug should be taken at bedtime, half an hour after a 15-minim dose (1 mil) of laudanum. Both emetin and crude ipecac often prove ineffectual in extremely acute and extremely chronic cases of amebiasis. In such cases, as well as in carriers, emetin-bismuth iodid, although it has a tendency to produce vomiting and diarrhea, is often of service. The usual dose is 2 to 3 grains (0.13–0.2 gm.) in salol-coated pills or in capsules, once daily preferably after the mid-day meal, for 10 or 12 successive days. Rest in bed for an hour or two after the administration of emetin-bismuth iodid is essential.

Irrigation of the bowel is frequently efficacious in chronic cases. It should be done once a day by means of a fountain-syringe and a long rectal tube, and with the patient in the knee-chest position or on his back with his hips well elevated. The best solution for the purpose is one of quinin bisulphate (1 to 5000 gradually increased to 1 to 1000) or one of silver nitrate (1 to 2000 gradually increased to 1 to 1000). From 1 liter to 2 liters should be allowed to enter slowly and the enema should be retained if possible ten or fifteen minutes. If the rectum is very irritable a small quantity of cocain solution (4 per cent.) may be introduced first. In intractable cases recourse may be had to colostomy or appendicostomy and irrigation of the colon through the wound.

ACTINOMYCOSIS

The treatment of an accessible lesion is by complete excision, or if this is impossible, by partial excision or curettement, followed by the application of iodine or of phenol and alcohol. Internally, potassium iodid is of definite value and should be used in all cases irrespective of other forms of treatment. To secure the best results it should be given in large doses, as much as 3 drams (12.0 gm.) daily. Bevan has recommended cupric sulphate, internally in doses of $\frac{1}{4}$ to $\frac{1}{2}$ grain (0.015–0.03 gm.) thrice daily, and locally in 1 per cent. solution (see p. 366). In the pulmonary form good results have been claimed for eucalyptus oil in spray and in capsules. A vaccine of the homologous organism, prepared by cultivating the fungus in nutrient broth to which a few drops of fresh human blood have been added, has sometimes proved serviceable (Wynn, Kinnicutt and Mixter, Gordon). Recently, roentgen ray or radium has been used in a number of cases with good results.

DISORDERS OF NUTRITION AND METABOLISM

SCURVY

Scurvy can be completely prevented by observing proper hygienic measures, and the eating of a sufficient quantity of fresh food. For use on shipboard, in camps, etc. potatoes, onions, beets, cabbage and certain fruits, particularly lemons, limes, or oranges, are valuable antiscorbutics. Generally speaking, heating, desiccation and oxidation lessen or destroy the antiscorbutic vitamin; nevertheless, canned tomatoes, dried orange juice or tomato juice, and milk that has been dried by being subjected to a temperature of 230° F. for only a few seconds possess considerably antiscorbutic potency. Pasteurization of milk apparently produces greater deterioration than boiling for a few minutes.

When scurvy has already developed rest and an abundance of fresh air and sunlight are important adjuvants to the dietetic treatment, which consists in giving generous amounts of fresh meat and fresh vegetables with several ounces of lemon, lime or orange juice daily. If the patient is unable to chew, owing to severe gingivitis, the diet must be limited to fresh milk, eggs, strong animal broths, purée of potatoes and fruit juices. Drugs are of secondary importance, although iron and bitter tonics, especially quinin, are often of value. The affected gums should be painted with a solution of silver nitrate—10 grains to the ounce (0.65 gm. —30.0 mils)—and the mouth should be washed at frequent intervals with a solution of potassium permanganate or potassium chlorate.

Infantile Scurvy.—In artificially fed infants scurvy can be prevented by using raw milk of good quality and suitably modified to the exclusion of heated milk and proprietary foods. If pasteurized milk must be used, the child should be given orange juice (1 tablespoonful daily) after the first month. In the treatment of the disease orange juice is a specific. The dose is from 1 to 2 tablespoonfuls daily. Purée of potato is also useful and may be substituted for the orange juice if there is diarrhea. Cod-liver oil and yeast have no antiscorbutic potency. The painful limbs should be kept warm.

RICKETS

Measures intended to promote the mother's health during the procreative period, good hygienic surroundings, and proper feeding are the important factors in prophylaxis. If the mother be deemed unfit for nursing and a suitable wet-nurse cannot be

procured, the diet must be given first attention. As a rule, clean, fresh unboiled cow's milk, properly modified to suit the age and digestive powers of the infant, is the best food. After the first six months beef juice and egg albumin may be added. Proprietary foods, if used at all, should be limited to periods of emergency. A small amount of fresh orange juice seems to be of service in some cases, even in the absence of any scorbutic taint. According to Hess, it is feasible to rid a locality of rickets by the systematic use of cod-liver oil. After the first year eggs, scraped beef and stale bread with butter should, as a rule, form a fairly large part of the diet. Foods rich in starch must always be used sparingly, especially if there is much abdominal distention.

Next to feeding, general hygienic measures are of the most importance. An abundance of fresh air and sunshine are always to be recommended, but precautions against chilling must not be neglected. It has been shown experimentally that exposure to direct sunlight, that is to sunlight that has not passed through window glass, has a pronounced therapeutic effect. A tepid bath (about 85° F. at 6 months) should be given once a day in a warm room and followed by friction of the surface or very gentle massage. In regard to drugs, cod liver oil not only benefits nutrition, but it definitely increases the capacity of the bones to take up or retain calcium. Phosphorus has also been well recommended, especially in combination with cod liver oil. The phosphorated oil, each minim of which represents $\frac{1}{100}$ grain (0.00064 gm.), may be given in doses of $\frac{1}{2}$ to 1 drop, three times a day. Remedies to correct faulty digestion are often required, and in anemic cases, iron, preferably in organic form, is clearly indicated. To avoid deformities, sitting up, standing and walking should be discouraged while the bones are soft. For the same reason the child should not be carried always on the same arm or allowed to lie continuously on one side.

OBESITY

The aim must be to diminish the supply or to increase the destruction of fat. The first aim is accomplished by restriction of food, and the second, chiefly, by properly regulated exercise. In whatever direction the effort at reduction is made, it must be recognized that a loss of weight in excess of one or at most 2 pounds a week is, as a rule, undesirable, and likely to be attended with nervous irritability, general weakness or other untoward effects. Especially important is it to see that the loss of proteins does not exceed the supply, at least for any considerable period. During the treatment the patient should be seen at brief intervals, so as

to afford frequent opportunities for taking and recording his weight, observing the effect of the reducing process on his general health, and making such modification in the dietetic and other regulations that changes in his condition may require. In arranging the diet an endeavor should be made to diminish the total quantity of nutritious food while at the same time admitting a sufficient bulk of palatable material to have a satisfying effect upon the appetite. The ingestion of fats, sugar and starches in particular must be limited, although other foods must also be taken in moderation. Ordinarily, the protein content of the diet should not be much less than 100 grams a day.

Green vegetables and tart fruits may be allowed in relatively liberal amounts, as they are bulky in proportion to their caloric content. Of course, the degree of restriction must be determined in each separate case by the results, and these are best judged by the weight and subjective sensations of the patient. Ordinarily, the total amount of calories may be safely reduced, at least for a time, to about one-half of that necessary to maintain an individual of the same age and sex as that of the patient, but of normal weight.

The patient must weigh each portion of meat, bread, etc. until he is able to judge accurately the amount that is permissible from its bulk. As a rule, the meals should be limited to three, but occasionally, it may be necessary to lessen the appetite by allowing raw fruit or a cup of bouillon in the intervals between meals or on retiring. Water should be restricted in amount and taken preferably between meals. Especially important is it to limit the entire amount of fluid taken in the twenty-four hours when there are indications of cardiac insufficiency.

Special dietetic measures may be of value in certain cases of obesity, if the patient can be kept in bed or at rest. Among these are the various modifications of the milk cure. Thus, a liter of milk may be given on two days of each week, and a more or less restricted general diet during the remainder of the week. Although the various milk cures are virtually starvation diets, they have the advantage of a restriction in the amount of fluids. Complete starvation, which is sometimes resorted to voluntarily by obese subjects, is the most rapid method of reducing weight, but to be perfectly safe, it must be in the form of a series of repeated fasts of increasing duration. Uninterrupted starvation is likely to cause within a day or two acidosis with headache, dizziness, nausea, etc. (Folin and Denis).

Muscular exercise constitutes the best method of promoting the destruction of fat already stored up in the tissues. It must be carefully graded, however, according to the strength of the patient. In many cases a brisk walk after each meal, the distance

being gradually increased, is the best form of exercise. It is scarcely necessary to add that vigorous muscular activity makes possible a more liberal dietary. For feeble patients the exercise may have to be limited to massage or passive movements. For robust subjects, cold bathing, followed by vigorous rubbing, is a valuable adjuvant to physical exercise.

Drugs are of minor importance. Thyroid extract is an active reducing agent, but unfortunately it causes a loss of protein as well as of fat. Occasionally, however, it acts well, but its effects must be carefully observed. Generally speaking, it produces the best results in cases of obesity showing evidences of disturbed endocrinous function. Ordinarily, the dose should not exceed 3 grains (0.13 gm.) of the dried gland two or three times a day. In cases apparently on the borderland between ordinary obesity and Fröhlich's adipositas cerebialis an extract of the anterior lobe of the pituitary gland may be of service. Saline cathartics have no special influence on the metabolism of fat, although they may bring about desirable subsidiary effects through their action on the bowel. When there are evidences of cardiac insufficiency, digitalis or strychnin, or both, will often prove useful. Finally, in extreme cases the excision of large pendulous masses of fat may occasionally seem advisable.

The following dietary may be taken as an illustration of what would be suitable at the beginning of treatment for a man who weighs 200 pounds and who should normally weight 165 pounds.

Breakfast

One orange or one-half grape fruit.....	about 80 calories
Two eggs, boiled or poached.....	about 160 calories
One ounce of wheat bread or rolls with an extremely small amount of butter.....	about 110 calories
One cup of coffee, with two teaspoonfuls of milk (not cream) and with one lump of sugar.....	about 44 calories

Dinner

Three ounces of clear soup.....	about 18 calories
Six ounces of lean meat (mutton, veal, beef or chicken), without gravy.....	about 342 calories
(Eight ounces of fresh fish—bass, trout, perch or cod—baked or boiled), may be substituted for other meat	
Four ounces of potatoes (white), baked, or boiled, and without butter.....	about 95 calories
Two ounces of one of the following vegetables: spinach, string beans, green peas, aspara-	

gus, tomatoes, turnips, prepared without butter.

Four ounces of fresh fruit.....about 50 calories

Luncheon

Four ounces of lean meat, baked, boiled or boiled, without gravy.....about 190 calories

(This may be replaced by one dozen small raw oysters.)

One cup of bouillon or clear soup.....about 18 calories

Salad or lettuce, celery, or tomatoes, any quantity, with vinegar or lemon juice, but no oil.....about 31 calories

One ounce of bread with a small amount of butter.....about 108 calories

Food material	Protein, grams	Fat, grams	Carbo- hydrate, grams	Calories
Breakfast				
Orange or half grapefruit.....	1.2	0.3	17.4	80
2 eggs.....	13.2	12.0	160
2 oz. wheat bread or rolls.....	2.6	0.3	15.0	75
Butter (small portion).....	0.04	5.5	35
Coffee.....				
Milk.....	0.06	0.8	1.0	14
Sugar, 1 lump.....	7.6	30
Lunch				
Lean meat (4 oz.).....	23.9	10.2	190
Bouillon (5 oz.).....	3.3	0.3	18
Lettuce.....	0.5	0.1	0.4	9
Tomato (1).....	0.5	0.3	3.0	16
Celery.....	1.4	6
Bread.....	2.6	0.3	15.0	73
Butter (small portion).....	0.04	5.5	35
Dinner				
Clear soup (5 oz.).....	3.3	0.3	18
Chicken (6 oz.).....	43.1	18.0	342
Trout (5 oz.).....	49.5	10.5	300
Potato (1).....	2.5	0.1	21.0	95
Choice of:				
Spinach.....	1.1	0.1	1.8	14
String beans.....	1.2	0.1	2.9	22
Green peas.....	38	0.2	9.8	57
Asparagus.....	1.0	2.0	13
Choice of:				
Strawberries (4 oz.).....	1.1	0.7	7.9	42
Apple (5 oz.).....	0.5	0.5	16.0	70
Banana (3½ oz.).....	0.8	0.4	14.0	64
	98.2	54.6	100.8	1273

Adiposis Dolorosa (Dercum's Disease).—Treatment is not very satisfactory. Thyroid extract, or a combination of thyroid extract and pituitary extract (anterior lobe), is sometimes of considerable benefit, however, in the early stages. Dietetic measures are not likely to be of service unless there is general obesity. Hydrotherapy and massage may be tried.

GOUT

The Acute Attack.—At the outset a brisk mercurial purgative, followed by a saline, is almost always advisable. The diet should be restricted to milk, eggs and farinaceous foods. The liberal use of water should be encouraged. Two drugs are especially efficacious, namely, colchicum and cinchophen (atophan). The former is used empirically; the virtue of the latter apparently depends upon its power to increase the excretion of uric acid. Tincture of colchicum seed may be given in doses of 30 minims (2.0 mls) every three hours or in amounts sufficient to cause slight looseness of the bowels. The alkaloid, colchicin, is equally effective. It may be given in doses of $\frac{1}{120}$ grain (0.0005 gm.) every four hours until the pain is relieved. The usual dose of cinchophen is about 7 grains (0.5 gm.) every four hours. It is best given in capsules, and should be accompanied by an alkali, preferably large doses of sodium bicarbonate, to prevent precipitation of the uric acid in the urine before it is passed. Otherwise, alkalis, formerly so much in vogue, have been largely abandoned. Nevertheless, large doses of the organic salts of potassium, especially the citrate, seem to do good. Occasionally, the pain of acute gout is so excruciating that the use of morphin becomes necessary.

The affected member should be elevated, immobilized, and enveloped in cotton wool or hot fomentations (hot saturated solution of magnesium sulphate). Cold applications, leeching, and blistering do not, as a rule, act well.

Chronic Gout.—No absolute rule can be laid down regarding the diet. The special features in each case should receive careful study. Some patients do well upon a non-protein diet, others do not. Simplicity and moderation are of the utmost importance. Generally speaking, a diet composed for the most part of milk, farinaceous foods, succulent vegetables, and eggs is most suitable. Owing to the difficulty that gouty patients have in excreting uric acid, it is advisable to exclude from the diet foods which are especially rich in purin bodies, such as sweetbreads, liver, kidneys, peas, beans, and lentils. Concentrated soups, hashes, croquettes, rich pastry, malt liquors, heavy wines and other alcoholic beverages

ages should also be avoided. So far as flesh is concerned, there is no difference between red and white meats, and usually either may be allowed once a day in moderation, unless a coexisting nephritis makes an extreme restriction in the protein intake necessary. Some patients are exceedingly intolerant of acid fruit. Tea and coffee, in moderation, do not appear to be particularly harmful, probably because methylated purins (caffeine, theobromin) are in large part destroyed within the body. Water-drinking between meals should be encouraged.

The quantity as well as the character of the food must be regulated. No more should be eaten than is absolutely necessary to satisfy hunger. The patient should be warmly clothed and should avoid as far as possible exposure to sudden atmospheric changes. Systematic exercise in the open air is very beneficial. Well-nourished patients should be urged to take walking trips, to play golf or tennis, or to try horseback riding. When active exercise is not feasible, massage may be strongly recommended. All overwork of mind should be forbidden. Hydrotherapy—tepid sponge-baths and douches—is useful. Heavy robust patients often derive much benefit from the Turkish bath.

Visits to certain mineral springs—Bedford, Saratoga, Harrogate, Carlsbad, Contrexeville, Aix-les-Bains—are sometimes of value. The good effects of the spa treatment are only in part due to the waters drunk; change of scene, fresh air, strict diet, and freedom from business and household cares are important factors. Residence during the winter months in a dry, warm, inland climate is desirable.

Remedies intended to improve the digestion are frequently indicated. In some cases a combination of an acid and a bitter before meals is of service. Daily action of the bowels should be secured. Of special remedies, those most worthy of consideration are colchicum and arsenic. Colchicum is most effective in the paroxysms, although small doses with alkalis may be of benefit in the intervals. The prolonged use of arsenic occasionally seems to do good. Gudzent, His, Klemperer and others report good results from the ingestion of water impregnated with radium emanation, but Rowntree and Baetjer in a small series of cases were not favorably impressed with the treatment, and McCrudden and Sargent were unable to demonstrate any influence from radium therapy on the uric acid content of the blood or on the rate of excretion of uric acid. So-called uric-acid solvents (piperazin, lycetol, quinic acid, etc.) are valueless.

DIABETES MELLITUS

The chief indications are to relieve the strain on the overtaxed pancreas and to render its function more effective by restricting the carbohydrate of the diet or, if necessary, restricting the total diet, thus reducing the volume of tissue to be served by the gland. In mild cases of diabetes the restriction of sugars and starches, and to a less extent of fat and protein, so that the entire food intake is well within the assimilative capacity of the patient is usually sufficient to remove both the glycosuria and the hyperglycemia.

Frequently in the milder cases a carbohydrate-free diet of 1500 to 1600 calories will soon render the patient aglycosuric, and after this has been accomplished and maintained for a few days it will be found possible to order starches in gradually increasing amounts. As a rule, however, it is advisable to maintain the carbohydrate level at 25 per cent. below that of the patient's maximum tolerance, to keep the fat within 200 grams and the total diet within 2200 calories and to introduce at intervals of a week or ten days a fast-day or a day in which the diet is restricted to 5 per cent. vegetables and one-half the usual quantity of fat and protein. The urine should be examined at frequent intervals—at first once or twice a week—and should glycosuria reappear, it should be checked by a return to the original carbohydrate free diet or a fast day. The following table, which is that compiled by Joslin, with slight modifications indicates the carbohydrate, fat and protein content of important foods and their caloric value.

DIET TABLE

Strict diet: Meats (except liver), fish (except roe), broths, eggs, butter, olive oil, coffee and tea, cheese, pepper, salt mustard, vinegar.

Water, clear broths, coffee, tea, cocoa shells can be taken without allowance for food content.

FOODS ARRANGED APPROXIMATELY ACCORDING TO CONTENT OF CARBOHYDRATES

	5 per cent.*		10 per cent.*	15 per cent.	20 per cent.
VEGETABLES (fresh or canned)	Lettuce	Tomatoes	String beans	Green peas	Potatoes
	Cucumbers	Brussels sprouts	Pumpkin	Artichokes	Shell beans
	Spinach	Water cress	Turnip	Parsnips	Baked beans
	Asparagus	Sea kale	Kohl-rabi	Canned lima beans	Green corn
	Rhubarb	Okra	Squash		Boiled rice
	Endive	Cauliflower	Beets		Boiled macaroni
	Marrow	Egg plant	Carrots		
	Sorrel	Cabbage	Onions		
	Sauerkraut	Radishes	Green peas canned		
	Beet greens	Leks			
	Dandelion greens	String beans canned			
	Swiss chard	Broccoli			
	Celery	Artichokes			
	Mushrooms	canned			
FRUITS	Ripe olives (20 per cent. fat)		Watermelon	Raspberries	Plums
	Grape fruit		Strawberries	Currants	Bananas
			Lemons	Apricots	Prunes
			Cranberries	Pears	
			Peaches	Apples	
			Pineapple	Huckleberries	
			Blackberries	Blueberries	
			Gooseberries	Cherries	
			Oranges		
Nuts	Butternuts		Brazil nuts	Almonds	Peanuts
	Pignolias		Black walnuts	Walnuts (Eng.)	
			Hickory	Beechnuts	40 per cent.
			Pecans	Pistachios	
Misc.	Clams	Oysters	Filberts	Pine nuts	Chestnuts
	Scallops	Liver			
		Fish roc			

* Reckon *actual available* carbohydrates in vegetables of 5 per cent. group as 3 per cent. of 10 per cent. group as 6 per cent.

(30 grams 1 oz.) Contain approximately	Carbo- hydrates, grams	Protein, grams	Fat, grams	Calories
Oatmeal, dry weight.....	20	5	2	120
Shredded Wheat.....	23	3	0	104
Cream, 40 per cent.....	1	1	12	120
Cream, 20 per cent.....	1	1	6	60
Milk.....	1.5	1	1	20
Brazil nuts.....	2	5	20	210
Oysters, six.....	4	6	1	50
Meat (uncooked, lean).....	0	6	3	50
Meat (cooked, lean).....	0	8	5	75
Bacon (cooked).....	0	5	15	155
Cheese.....	0	8	11	135
Egg (one).....	0	6	6	75
Vegetables, 5 per cent. group.....	1	0.5	0	6
Vegetables, 10 per cent. group.....	2	0.5	0	10
Potato.....	6	1	0	30
Bread.....	18	3	0	90
Butter.....	0	0	25	225
Oil.....	0	0	30	270
Fish, cod, haddock (cooked).....	0	6	0	25
Broth.....	0	0.7	0	3
Fruit, 10 per cent.....	3	0	0	12

1 gm. protein, 4 calories.

1 gm. fat, 9 calories.

1 gm. carbohydrate, 4 calories.

30 gm. alcohol, 7 calories.

30 gm. = 1 ounce.

1 kilogram = 2.2 pounds.

A patient "at rest" requires from 25 to 30 calories per kilogram body-weight. Growing children may require 50 calories or more per kilogram.

In severe cases the urine cannot be rendered sugar free by a partial reduction of the diet and recourse must be had to a more drastic method of treatment, such as that of prolonged fasting, originally suggested by Guelpa, and later elaborated and put on a rational basis by Allen. The points emphasized by Allen are the importance of quickly relieving the pancreatic strain by prolonged fasting, the insidiously harmful effect of a long-continued diet rich in fat, and the necessity of maintaining pancreatic rest even at the expense of the body-weight. Joslin gives the following excellent summary of the fasting treatment.

Preparations for Fasting.—In severe, long-standing cases, obese and elderly cases, as well as in all cases with acidosis, or in any case if desired, without otherwise changing habits or diet, omit fat, after two days decrease protein and halve the carbohydrates daily until the patient is taking 30 grams or less; then fast. In other cases begin fasting at once.

Fasting.—Fast four days, unless earlier sugar-free. Allow water freely, tea, coffee, and thin clear meat broths as desired.

Intermittent Fasting.—If glycosuria persists at the end of four days, give 1 gram protein or 0.5 gram carbohydrate per kilogram body-weight for two days and then fast again for three days, unless earlier sugar-free. If glycosuria remains, repeat and then fast for one or two days as necessary. If there is still sugar, give protein as before for four days and then fast one, and then gradually increase the periods of feeding, one day each time, until fasting one day each week.

Carbohydrate Tolerance.—When the 24-hour urine is free from sugar give 5 or 10 grams carbohydrate (150 to 300 grams of 5 per cent. vegetables) and continue to add 5 or 10 grams carbohydrate daily (more in mild cases) up to 50 grams or more until sugar appears, then fast until sugar free.

Protein Tolerance.—When the urine is again sugar-free decrease the carbohydrate by one-third below the carbohydrate tolerance or at least 10 grams, and then add about 20 grams protein and thereafter 15 grams daily in the form of egg-white, fish or lean meat (chicken) until the patient is receiving from 1 gram to 1.5 grams protein per kilogram body-weight.

Fat Tolerance.—It is usually desirable, especially in the young, to add no fat until the protein reaches 1 gram to 1.5 grams per kilogram body-weight and the blood sugar is normal. Then 5 to 25 grams daily according to previous acidosis until the patient ceases to lose weight or receives in the total diet 20 to 30 calories per kilogram body-weight.

Reappearance of Sugar.—The return of sugar demands fasting for 24 hours, or until sugar-free. Resume the former diet adding fat gradually and last of all in order to maintain as high a carbohydrate tolerance as possible, sacrificing body weight for this purpose.

Weekly Fast Days.—Whenever the tolerance is less than 20 grams carbohydrate, fasting should be practised one day in seven; when the tolerance is over 20 grams of carbohydrate cut the diet in half on one day each week.

The foods commonly employed in determining the tolerance for carbohydrate and protein are 5 per cent. vegetables, oranges, grape-fruit, oatmeal or shredded wheat, potato, fish, chicken, lean meat, skimmed milk.

During the fasting period weak patients should remain in bed. For vigorous patients exercise is indicated, as it seems to increase carbohydrate tolerance. Pronounced fatigue, however, must always be avoided. Alcohol, to the extent of 3 or 4 ounces (90–120 mls) of whisky or brandy a day, may be given during the fast, although it is not usually necessary. Water may be allowed in any amount and tea, black coffee, and clear broth in moderation. In some cases modifications of the treatment are necessary. If the patient is unable to utilize the small amount of carbohydrate contained in the green vegetables, these may be boiled in three changes of water, and the latter discarded. Tuberculosis is not in itself a contraindication to

fasting treatment, as the removal of glycosuria and acidosis is of primary importance; nevertheless in some instances the results are not good.

Not rarely, treatment by undernutrition requires modification because hypoglycemia (below 0.06 per cent.), which is of ill omen, supervenes (Joslin) or because complete fasting does not make the patient sugar free. Woodyatt, Newburgh and others have recently shown that a diet of 900 calories, derived chiefly from fat, is as effective in rendering the patient sugar free and in reducing basal metabolism as starvation, and, moreover, that it is less dangerous to the patient and much less of a hardship. The diet advocated by them, and which often yields good results, even in severe cases, is one of low carbohydrate, low protein and high fat (2 grams per kilogram of body weight).

A stay of 2 or 3 weeks in an institution at the beginning of treatment is very desirable, for during this period the patient can be taught how to readjust his life and made to understand the necessity of being under supervision. If sufficiently intelligent, he can be taught, also, how to examine his own urine and how to estimate the intake and output of carbohydrate. Whatever plan of low-maintenance is primarily adopted, eventually the caloric intake should be so adjusted, if possible, that ketones and sugar do not reappear in the urine and that the patient neither gains in weight nor suffers any progressive loss of weight. Ordinary bread is rarely allowed, but substitutes made of gluten flour of known composition, such as Akoll biscuits, may be used. To fill the stomach bran biscuits* may be ordered. Tea, coffee, gelatin jellies, etc. may be sweetened, if necessary, with saccharin, although the persistent use of this drug sometimes results in indigestion.

Drugs have not proved of much value in diabetes. Recently, however, Macleod and his associates, at the University of Toronto, have prepared a pancreatic extract, tentatively termed "insulin," which inhibits the hyperglycemia in animals resulting from extirpation of the pancreas, piqûre of the fourth ventricle, etc. Whether this preparation can cure or only relieve diabetes

* The recipe used at the Rockefeller Institute Hospital is:

Bran.....	60 gm.
Salt.....	$\frac{1}{4}$ teaspoonful
Agar agar, powdered.....	6 gm.
Cold water.....	100 mls ($\frac{1}{2}$ glass)

Tie bran in cheese cloth and wash under cold water tap until water is clear. Mix agar agar in the water (cold) (100 mls) and bring to the point of boiling. Add to washed bran the salt and agar agar solution (hot). Mold into three cakes. Place in pan and, when firm and cold, bake in moderate oven from 45 to 50 minutes.

in man has not been definitely determined, but the clinical experiments thus far undertaken indicate that it is a remedy of great value. Opium in crude form or its alkaloid codein promotes comfort by obtunding perceptions and may diminish slightly the glycosuria by retarding the absorption of carbohydrates, but its use is inadvisable except in hopeless cases. Tonics are sometimes indicated. Constipation, which is baneful, if not relieved by food substitutes (bran, agar agar, etc.) must be combated by vegetable or saline cathartics. Courses of bromids are sometimes of service in controlling nervous manifestations. All rules conducive to good health should be followed as closely as possible and especial care should be taken to avoid infections, even common "colds."

Most of the complications of diabetes are controlled or greatly benefited by strict dieting. Diabetes does not modify the usual principles of surgical procedure, in such conditions as gangrene and cataract, although operations of all kinds are, of course, rendered more dangerous by the disease. If a general anesthetic is required ether and chloroform should be avoided and nitrous oxid-oxygen employed. Boils usually yield to vigorous anti-diabetic treatment. Pruritus of the genitals may be relieved by anointing the parts freely with petrolatum before urination or protecting them with zinc stearate. General pruritus may require the use of a wash containing phenol, resorcinol or boric acid (see p. 407).

Diabetic Coma.—If coma is impending and the patient has been on an ordinary diet, a moderate amount of carbohydrate in the form of thin oatmeal gruel made with water (60 grams of oatmeal each 24 hours for a patient weighing 150 pounds) should be ordered. Sodium bicarbonate seems to be helpful in replenishing the alkali reserve, although Joslin believes that it does more harm than good. It may be given by the mouth (4 to 6 gm. or more in weak solution) every 2 hours or by the rectum (3 to 5 per cent. solution). In urgent cases, however, it is best given intravenously (not subcutaneously) in 4 per cent. solution made with freshly sterilized water. For an adult 500 mls or more may be injected every few hours. A neutral reaction of the urine or, better, a normal blood CO_2 reading, is an indication that sufficient alkali has been given. Solutions of sodium bicarbonate should not be boiled as the heat tends to transform the bicarbonate into carbonate, which is injurious. Whether alkali is used or not, a large amount of fluid (1000 mls within each 6 hours) should be prescribed. The fluid may be taken by the mouth as water, tea, coffee or thin broths, or by the rectum or intravenously in the form of normal saline solution. Nausea

must be avoided and every effort that excites it should be suspended. Free evacuation of the bowels is necessary and may be secured by calomel and salts or by enema.

DIABETES INSIPIDUS

The patient should have a nutritious but easily digestible diet and should be placed under favorable hygienic conditions. It is not advisable to restrain him much in the matter of drink, except in the evening when the intake of fluid should be reduced, so as to avoid interference with sleep. A salt-poor diet is sometimes beneficial. Arsphenamin, mercury and iodids should be given a thorough trial whenever there is evidence of syphilis. Subcutaneous injections of an extract of the posterior lobe of the pituitary body (1 mil once a day) often give great relief, although the action of the drug rarely lasts more than 24 hours. Oral administration is ineffectual. In a few cases reported by Herrick Cammidge, Graham, Tucker and others lumbar puncture was followed by marked improvement or actual cure. Among special remedies that have been extolled from time to time may be mentioned valerian ($\frac{1}{2}$ –1 fluidounce—15–30 mils—of the ammoniated tincture daily), ergot (10 minims—0.6 mil of the fluidextract three times a day), strychnin sulphate ($\frac{1}{30}$ – $\frac{1}{20}$ grain—0.002–0.003 gm.) two or three times a day hypodermically, and the bromids.

DISEASES OF THE DIGESTIVE TRACT

STOMATITIS

The underlying cause of the disease must be removed. Digestive disturbances should receive careful attention. The general health of the patient should be improved by dietetic measures and, if necessary, by the administration of tonics. In infants cleansing of the mouth and of the mother's nipples, or of artificial nipples, if these are being used, is imperative. In the *catarrhal* and *aphthous* forms of stomatitis, mild antiseptic mouth-washes, such as a 5 per cent. solution of boric acid with 5 per cent. of glycerin will usually suffice. In refractory cases the mouth may be painted with a 1 per cent. solution of silver nitrate or, if there are ulcers, these may be touched with a 5 or 10 per cent. solution of the salt.

In *ulcerative stomatitis* the ulcers may be carefully painted with a 10 per cent. solution of silver nitrate or, in case of infection with the organisms of Vincent's angina, with undiluted Fowler's solution (three or four times a day) or with arsphenamin. A

1 to 1000 solution of potassium permanganate or the official solution of hydrogen dioxid, diluted with 2 or 3 parts of water, makes a good mouth-wash. Internally, potassium chlorate is in many cases a specific. The dose for a child of 3 or 4 years is from 1 to 3 grains (0.06–0.2 gm.), in dilute solution, every 3 or 4 hours. In severe cases of Vincent's angina intravenous injections of arsphenamin, in doses of 1 to $1\frac{1}{2}$ grains (0.06–0.1 gm.), at intervals of 3 or 4 days, has proved curative.

Thrush usually yields to local applications of an alkaline solution, such as one of sodium bicarbonate or sodium biborate, 10 grains (0.65 gm.) to the ounce (30.0 mls). The applications should be made gently but thoroughly with absorbent cotton or a soft piece of rag wrapped around the index finger after each feeding. To prevent reinfection, the mother's nipples, or if the infant is bottle-fed, both the nipple and the bottle, must be thoroughly cleansed before and after each feeding.

In *gangrenous stomatitis* (*cancrum oris*) the diseased tissue should be destroyed under anesthesia with the actual cautery or nitric acid. After the operation the mouth should be cleansed at frequent intervals with a solution of hydrogen dioxid (1:3) or potassium permanganate (1 per cent.). Externally, wet dressings of Carrel-Dakin solution or of diluted alcohol should be employed. If diphtheria infection is proved by culture, diphtheria antitoxin should be used. Concentrated nourishment and general stimulants are indicated.

ACUTE TONSILLITIS

In all but the mildest cases the patient should remain in bed. Isolation is always desirable, and when there is a suspicion that the case is one of diphtheria or scarlet fever it is imperative. A mild aperient is indicated at the outset. The sucking of ice affords relief. The most reliable internal remedies are the salicylates and benzoates. One of these should be given in full doses at frequent intervals.

℞. Tincturæ aconiti..... ʒxl (2.5 mls)
 Sodii salicylatis..... ʒiiss (6.0 gms.)
 Syrupi aurantii..... f ʒi (30.0 mls)
 Aquæ..... q. s. ad f ʒiii (90.0 mls).—M.
 Sig.—A dessertspoonful every 2 or 3 hours.

If given early, biniodid of mercury— $\frac{1}{200}$ grain (0.0003 gm.) in water every hour for 5 hours—is sometimes useful, especially in follicular tonsillitis. Occasionally the pain is so severe as to require the use of morphin.

Local Treatment.—Externally cold applications often afford more relief than fomentations. Mild antiseptic solutions, such as Dobell's solution or a solution of hydrogen dioxid (1:4) are beneficial. Direct applications to the surface of the glands of argyrol (10–20 per cent. solution), of dry sodium bicarbonate, of finely powdered acetylsalicylic acid, or of the tincture of ferric chlorid are often useful.

℞. Potassii chloratis..... gr. xx (1.3 gm.)
 Tincturæ ferri chloridi..... f ʒiii (12.0 mls)
 Glycerini..... f ʒiv (15.0 mls)
 Aquæ..... q. s. ad f ʒii (60.0 mls)
 Sig.—Use locally.

When the swelling is pronounced, scarification, followed by gargling with hot water, is another measure that sometimes affords relief.

Pus should be evacuated as soon as its presence can be detected. In the large majority of cases it is best to make the incision not in the tonsil itself, but in the soft palate, a little above and to the outer side of gland, or at the intersection of an imaginary line drawn horizontally across the base of the uvula and one drawn vertically along the anterior faucial pillar.

CHRONIC TONSILLITIS

The only treatment of septic tonsils is complete tonsillectomy and this operation is especially advisable if there are evidences of secondary infection elsewhere in the body or the patient's general health is becoming affected. It is contraindicated, however, during the course of superimposed acute tonsillitis. Treatment by astringent and antiseptic applications invariably fails and incomplete tonsillectomy may aggravate the local condition and favor dissemination of the infection. Pharyngeal adenoids must also be removed by operation. In addition, it is usually necessary to apply general hygienic measures and to administer tonics, such as iron, arsenic and cod liver oil, so as to increase the patient's vigor and resistance.

ACUTE CATARRHAL PHARYNGITIS

Acute catarrhal pharyngitis usually occurs in association with acute tonsillitis, and is uncommon as an independent condition. Locally, a cleansing gargle of normal salt solution or of dilute Dobell's solution, every four hours is useful. An oily spray, consisting of 2 grains (0.13 gm.) of menthol to the ounce (30.0 mls) of liquid petrolatum, is also efficacious. Externally,

cloths wrung out of cold water or an ice-bag afford relief. It is desirable to have the bowels moved freely at the onset, using a cathartic for the purpose, if necessary. If the pain and fever are marked a benzoate or salicylate may be given in combination with acetphenetidin, as in the following formula:

R̄. Sodii benzoatis..... ʒii (8.0 gm.)
 Acetphenetidini..... gr. xl (2.6 gm.).—M.
 Fiant chartulæ No. xii.
 Sig.—One powder every three hours.

CHRONIC PHARYNGITIS

Removal of the cause is of prime importance. All sources of local irritation, such as overuse or misuse of the voice, mouth-breathing, excessive smoking and intemperance in eating and drinking, must be avoided. Patients should be instructed to expel sounds by the aid of the diaphragm and abdominal muscles instead of the muscles of the throat. Nasal obstructions and adenoid growths must be removed. The habit of hawking and scraping to clear the throat should be rigidly interdicted. Digestive disturbances should receive careful attention. Tonics are sometimes required.

The nasopharynx should be kept clean by the local use of mild, antiseptic alkaline solutions. Astringent applications, such as silver nitrate—5 or 10 grains to the ounce (0.3–0.6 gm. to 30.0 mils) or zinc sulphate 5 grains to the ounce (0.3 gm. to 30.0 mils) are sometimes of service. In the follicular form it is advisable to destroy the enlarged follicles by means of the galvanocautery, before making use of the astringent applications.

ACUTE GASTRITIS

If the stomach still contains irritating matter this should be removed at once by lavage, or the administration of ipecacuanha by the mouth or of apomorphin hypodermically. The application of a mustard-plaster or of a turpentine stupe over the region of the stomach will aid in relieving distress. As a rule, all food should be withheld for 24 or 36 hours. At the end of this time, milk and lime-water, pancreatinized milk, or light broths may usually be allowed in small quantities, at frequent intervals. The return to solid food should always be effected very gradually. Rectal feeding is rarely required. Thirst is best controlled by the use of cracked ice or, if necessary, by the administration of normal salt solution by the rectum. Rinsing the mouth with cold water at frequent intervals is both grateful and useful.

If there is constipation or any evidence that the irritant has passed into the bowel a mercurial laxative may be given and followed by magnesia or a Seidlitz powder. Vomiting may be relieved by bismuth subcarbonate, 10 grains (0.6 gm.) or cerium oxalate, 5 grains (0.3 gm.), every 2 hours. A combination of bismuth subnitrate with hydrocyanic acid (see p. 175) is often serviceable. Persistent vomiting, especially if accompanied by severe pain, may require an opium suppository or a hypodermic injection of morphin. During convalescence a bitter stomachic may often be taken with advantage. Such a combination as the following may be prescribed:

R. Sodii bicarbonatis..... ʒi (4.0 gm.)
 Tincturæ mucis vomicæ..... f ʒss (2.0 mls)
 Infusi gentianæ..... q. s. ad f ʒiii (90.0 mls).—M.
 Sig.—A dessertspoonful before meals.

In *acute toxic gastritis* the first indication is to remove the irritant, or to neutralize it by administering an appropriate antidote. An emetic may be given, but unless there is evidence of extensive corrosion, siphonage with the stomach-tube is preferable. In many cases the antidote may be given through the tube. In general, acids are neutralized by alkalis (magnesia, chalk, sodium bicarbonate) and egg-albumin, and alkalis by weak acids (vinegar, lemon-juice). Morphin is often required on account of the intense pain. Collapse must be combated by the application of heat to the surface of the body and by the subcutaneous administration of diffusible stimulants. The after treatment is that of the severer forms of acute catarrhal gastritis.

CHRONIC GASTRITIS

The cause should be ascertained and removed if possible. Regularity in the time of meals and thorough mastication of food must be insisted upon. The patient should be cautioned against overeating and the drinking of large quantities of liquid especially iced water, during meals. The resumption of mental or physical work immediately after meals must also be avoided. Change of scene, with freedom from business worry or household cares, and properly regulated exercise in the open air are often most desirable.

In general a mixed diet of soft, pulpy, or finely divided food should be prescribed. It may include, as a rule, boiled, baked, or grilled beef and mutton, boiled or baked chicken, boiled fish, stewed sweet-breads, soft-boiled or poached eggs, well-cooked rice, purée of potato, green peas or spinach, stale bread, fresh butter, calve's-foot jelly, junket and light puddings. Pork, veal,

smoked fish, fried foods, coarse vegetables, rich soups, strong spices, cheese, raw fruits, pastry, and sweetmeats should be avoided. Alcohol is inadmissible and tea, coffee and cocoa should be used sparingly, if at all. Ordinarily three meals a day will suffice, but if the motor power of the stomach is much impaired, it is better to give small meals at frequent intervals. In advanced cases, provided there is no marked atony of the stomach, it may sometimes be advisable to restrict the diet to milk or to milk with gruel, meat-jellies and minced beef. The milk (about two quarts in the 24 hours) should be taken at regular intervals and preferably diluted with lime-water.

Lavage of the stomach before breakfast may be of service if there is excessive secretion of mucus, otherwise this procedure should be reserved for the exceptional cases in which stagnation of the stomach-contents is present as a complication. Simple luke-warm water, a 1 per cent. solution of sodium chlorid, or 5 per cent. solution of sodium bicarbonate may be employed for the purpose. In some cases the sipping of a glassful of hot alkaline water half an hour before meals proves an efficient and agreeable substitute for lavage.

In chronic gastritis with subacidity, dilute hydrochloric acid, in doses of 10 minims (0.6 mil) gradually increased to 15 minims (1.0 mil), in a wine-glassful of water, taken through a glass tube, during or at the close of the meal is often of service. As such doses of the acid rarely suffice to compensate for the existing deficiency in acid secretion it is likely that the drug merely acts as a stomachic. Digestive ferments, such as pepsin and pancreatin, need not be given unless there is evidence of atrophy of the gastric follicles. The addition of a bitter—*nux vomica* or gentian—to the acid, however, is sometimes advantageous, especially if the appetite is poor or the stomach is atonic. If the stomach is irritable, bismuth subnitrate, in doses of 20 to 30 grains (1.3–2.0 gm.), suspended in water and taken half an hour before meals, is useful. If however, the irritability is associated with hyperacidity, better results may be secured by giving an antacid powder, such as the following, from $\frac{1}{2}$ to 1 hour after meals:

R_x. Bismuth subcarbonatis..... gr. ccl (16.0 gm.)
 Sodii bicarbonatis..... gr. cc (12.5 gm.)
 Magnesii oxidi..... ʒiiss (6.0 gm.)

Ft. chart. No. xx.

Sig.—One powder suspended in water half an hour after meals.

Not rarely, when the stomach is especially sensitive a short course of silver nitrate is of benefit. It may be given in pill form with extract of *hyoscyamus*, as in the following formula:

R. Argenti nitratis..... gr. vii (0.5 gm.)
 Extracti hyoscyami..... gr. xii (0.8 gm.)
 Fiant pilulæ No. xx.
 Srg.—One pill half an hour before meals.

Flatulence, if not relieved by appropriate diet, may yield to the administration of antifermentatives, such as creosote or phenol, in small doses. So far as possible, constipation should be overcome by regulation of the diet, exercise, massage and, perhaps, the occasional use of laxative enemas or suppositories. Should these measures fail sodium phosphate, Rochelle salt or artificial Carlsbad salt may be given in small doses in the early morning, preferably in hot water. Drastic purgatives, of all kinds are contraindicated.

HYPERCHLORHYDRIA AND GASTRIC HYPERSECRETION

The chief indications are to remove the underlying cause of the condition, to lessen the morbid impressionability of the nervous system, and to prevent any direct irritation of the stomach. Regular meals, regulation of the temperature of the food and drink, thorough mastication, avoidance of excesses in eating, drinking and smoking are cardinal points. Thorough mastication is especially important, for the more comminuted the food, the more bland it is, the more acid it binds, and the shorter its stay in the stomach. Although the patient is temporarily more comfortable upon protein foods, experience has shown that the best diet is a liberal mixed one of nutritious, bland, easily digestible food. Foods to which vinegar and spices have been added and highly seasoned dishes of all kinds must be interdicted. Fats in the form of butter, cream and olive oil, usually prove acceptable and efficacious. They not only depress acid secretion (Boas, Pawlow, Bachmann and others) but they also cause an actual reduction of acidity by inviting a regurgitation of the alkaline duodenal contents into the stomach. Tea and coffee should be used sparingly, if at all. Alcohol is usually inadmissible. Water-drinking at meals, provided it is not excessive and the temperature of the water is not too low, is not objectionable. Excessive smoking is distinctly harmful.

Alkalis in the form of sodium bicarbonate, magnesia, or chalk, administered at the height of digestion, almost invariably afford temporary relief. For securing more permanent effects bismuth subcarbonate in doses of 20 grains (1.3 gm.) or more, or silver nitrate in doses of $\frac{1}{6}$ to $\frac{1}{2}$ grain (0.01–0.03 gm.), with extract of hyoscyamus or belladonna, half an hour before meals is often useful. Sedatives, such as the bromids, are sometimes of service.

In hyperchlorhydria the result of brain tire, travel properly directed, often accomplishes much more than any form of medicinal or dietetic treatment, and may be confidently recommended to those who can afford it.

ATONY OF THE STOMACH

The first indication is to eliminate the causal factor. The food should be readily digestible, small in bulk, finely divided and nutritious. Fluids, except in moderate quantities, and coarse vegetables are to be avoided. The diet may include tender meats, eggs, oysters, boiled fish, well-cooked cereals, steamed rice, purée of potato, spinach or peas, stale bread and fresh butter. It is rarely necessary to increase the number of meals. Rest for at least an hour after large meals is to be recommended. Exercise in the open air and frequent bathing with friction of the skin are general measures of value. Lavage is unnecessary unless the condition has resulted in dilatation of the organ.

General tonics, especially iron, are often needed. The most useful direct remedies are the bitters (quassia, gentian, calumba), particularly the tincture of *mux vomica*, which may be given in doses of from 5 to 10 minims (0.3–0.6 mls), gradually increased to 15 or even 20 minims (1.0 to 1.3 mls), before meals. Alkalis are indicated when there is excessive acidity. Antifermentatives, particularly small doses of creosote, phenol, or betanaphthol, are useful in reducing flatulence. In cases with marked fermentation and heart-burn the following may often be used with advantage:

R. Phenolis..... ℥vi (0.4 mil)
 Sodii bicarbonatis..... ℥ii (8.0 gm.)
 Spiritus ammoniæ aromatici..... f ℥iv (15.0 mls)
 Spiritus chloroformi..... f ℥iss (6.0 mls)
 Aquæ menthæ piperitæ.... q. s. ad f ℥iii (90.0 mls).—M.
 Sig.—One teaspoonful after meals and at bed time.

Constipation is best relieved by regulation of the diet, abdominal massage and enemas.

ULCER OF THE STOMACH AND DUODENUM

Prolonged rest and an appropriate diet are the most important factors in the medical treatment of peptic ulcer. In chronic ulcer the rest should be kept up for from 6 to 10 weeks or even longer, and for the first 3 or 4 weeks of this period the patient should be confined to bed. As to the dietetic treatment, various

plans have been suggested, but none is suitable for every case. A method of procedure that is successful in many instances consists in rectal feeding or in the use of saline or glucose (5-10 per cent.) enemas (250 mls), by rectal drip, three times a day, for the first 3 or 4 days, followed by the administration of milk and cream and soft food in increasing amounts by the mouth. During the period of rectal feeding ice may be held in the mouth, if there is much thirst, but no water should be swallowed. To lessen the risk of parotitis the mouth may be washed at frequent intervals with an antiseptic solution. When feeding by the mouth is resumed, it is advisable to begin with milk or albumin-water, giving at first not more than 2 or 3 ounces every two hours. If milk is selected it should be diluted with lime-water. In the course of a few days cream, cream soups, beef juice, soft boiled eggs and well-cooked gruel may also be given. At the end of two or three weeks the intervals between the meals may be increased to three hours, and such articles as milk toast, boiled sweetbread, scraped beef, tender parts of oysters, white meat of chicken, vegetable purées, and custard pudding may be allowed. After 6 or 7 weeks tender beef or mutton, boiled fish, steamed rice, stale bread without crust, and a liberal quantity of butter may usually be added. The return to the ordinary mixed diet, with three meals a day, must be effected with caution and for at least a year after recovery coarse and rich food of every kind, as well as acids and spices, should be avoided.

The plan of treatment devised by Sippy often yields good results when the gastric acidity is high. It aims at reducing the acid content by appropriate food and alkalis every hour during the greater part of the day and the removal at night of any products of continuous hypersecretion. For the first 5 days no food or drink is given by the mouth, but about 12 ounces of normal salt solution is given per rectum 4 times daily. At the end of this period $\frac{1}{2}$ ounce each of milk and cream is given every hour from early morning until 8 or 9 o'clock at night. Half an hour before feeding is begun $\frac{1}{2}$ teaspoonful of bismuth subnitrate is given in half a glass of water, and midway between each feeding a powder consisting of 10 grains (0.65 gm.) each of magnesia and sodium bicarbonate are given alternately with a powder of 10 grains (0.65 gm.) each of bismuth subnitrate and sodium bicarbonate. If there is no discomfort the milk and cream are increased to 1 ounce on the second day and to $1\frac{1}{2}$ ounces on the third day. After two or three days more a soft egg may be added in the forenoon, and again in the afternoon, if desired. If there is no discomfort, the following day 3 ounces of a well-cooked cereal or a soft egg may be added. After a day or two another egg

or cereal portion may be added. The total bulk at one feeding should not exceed 6 ounces, when feeding every hour, and the number of eggs and quantity of cereal should depend on the individual requirements. At the end of three or four weeks, if desired, a small quantity of stewed fruit or jelly may be given. During the fourth week the interval between the feedings may be gradually increased, so that by the fifth week food is taken every 2 hours, no more than 8 ounces, however, being taken at one time. During this period milk toast, various vegetable purées and bread may be taken, if desired. After 2 or 3 weeks more, feeding every 3 hours may be established. During a period of a year or more, milk, cream, cereals, soft eggs, vegetable purées, cream soups, bread and butter, and meats, when desired, should form the basis of the diet.

The most useful drugs are the alkalis, the insoluble salts of bismuth, and silver nitrate. The alkalis are of service in reducing acidity and lessening motor activity. Sodium bicarbonate is one of the best; it should be given midway between each feeding and may be combined with magnesia or bismuth subcarbonate. A dose of from 10 to 15 grains (0.6–1.0 gm.) of each is usually sufficient. Carlsbad salt (sodium chlorid, 1 part; sodium bicarbonate, 2 parts; and sodium sulphate, 5 parts) is an excellent alkaline laxative, of which a teaspoonful or more may be taken in hot water in the early morning. The bismuth salts and silver nitrate act as protectives. From 15 to 20 grains (1.0–1.3 gm.) of bismuth subcarbonate, stirred in water, may be given on an empty stomach several times a day. As an alternate, silver nitrate may be given in doses of $\frac{1}{4}$ to $\frac{1}{2}$ grain (0.016–0.03 gm.), three or four times a day, before eating. Extract of belladonna or of hyoscyamus makes a good excipient for the silver salt. If the pain is especially severe belladonna itself may be given in doses sufficient to produce a definite physiologic effect. By depressing the vagus, it lessens both the motor and secretory functions of the stomach.

Iron, preferably in organic form, is useful in combating anemia. As it is not improbable that infection plays a part in producing and maintaining peptic ulceration, septic foci in the gums, about the roots of the teeth, or in the tonsils should always receive appropriate treatment. In the event of severe hemorrhage a light ice-bag should be placed over the stomach, morphin should be administered hypodermically, and from 20 to 30 drops of a 1:1000 solution of epinephrin should be given by the mouth every twenty minutes for two or three doses. The application of firm bandages to the four extremities may act favorably. Ewald and Minkowski have recommended irrigation of the stomach with

ice-water, and Weil and Rodman lavage with hot water (120°–130° F.). Collapse from hemorrhage will require the external application of heat, transfusion of blood or subcutaneous or intravenous injections of salt solution, and the hypodermic injection of diffusible stimulants. Probably no single hemorrhage, whatever its quantity, warrants immediate surgical intervention, and certainly in no case should an operation be done during the bleeding.

Surgical Treatment.—In all cases of acute perforation an operation should be done at the earliest possible moment. Patients treated surgically within 6 hours usually recover, while the large majority of those operated on after 12 hours die. Chronic perforation with perigastric abscess or an accessory pocket, persistent stenosis of the pylorus, organic hour-glass constriction of the stomach, repeated copious hemorrhages, any evidence of carcinomatous change, and the continuance of the symptoms after a thorough trial of appropriate medical treatment are also definite indications for operative treatment. Whether the surgical procedure shall consist of gastro-enterostomy, partial gastrectomy or pyloroplasty must be determined by the situation and extent of the ulcer. At the Mayo Clinic the operative mortality in 545 cases of gastric ulcer was 4.5 per cent. and in 1684 cases of duodenal ulcer, 2 per cent. Moynihan reports 808 operations for gastric or duodenal ulcer with a mortality of 1.23 per cent. Operations by competent surgeons afford complete and lasting relief in about two-thirds of all cases. Gastro-enterostomy sometimes fails owing to the occurrence of ulceration at the site of the anastomosis, the development of a jejunal ulcer below the anastomosis, the persistence of the original ulcer, occlusion of the artificial stoma, or the formation of adhesions. Whatever surgical procedure is employed, it is absolutely necessary to continue treatment along medical lines for several months after the operation or until permanent cure is assured.

CARCINOMA OF THE STOMACH

Medical Treatment.—In the early stages of the disease, if the pylorus is still patulous, a mixed diet of readily digested food is often well borne. Later, when there is retention, food should be selected that will make small demands on the stomach and that will leave little residue. Bitters—calumba, nux vomica, gentian—are sometimes employed with advantage. In many cases hydrochloric acid and pepsin are useful. Lavage affords the best means of relieving the distressing symptoms that result

from retention. Vomiting not dependent upon retention may be treated with such remedies as carbonated water, bismuth subnitrate, cerium oxalate and hydrocyanic acid. In refractory cases rectal feeding may be required for a time. Acid eructations and flatulency are sometimes relieved by antacids and antiseptics, but, as a rule, lavage is more effective. Severe pain will require opium, local sedatives, such as hydrocyanic acid, cocain and chloroform, and hot applications.

Surgical Treatment.—An exploratory operation is advisable in persons past 40 in whom pronounced digestive disturbances arise without obvious cause and persist despite an appropriate diet and medical treatment, especially if hypochlorhydria or achlorhydria, food retention, occult bleeding or abnormality of the gastric contour, as shown by x-ray, are among the manifestations. Pylorectomy or partial gastrectomy offers hope of a considerable prolongation of life and even of an actual cure when done at an early stage of the disease. Removal of the cancer-bearing area, however, is contraindicated when there is evidence of metastasis to any of the accessible lymph nodes, as those above the left clavicle, at the umbilicus or in the rectal shelf, or to any of the other organs, or when there are signs of free fluid in the peritoneum. The presence of a palpable tumor is not in itself a sign of inoperability, especially if it is movable. In cases of irremovable cancer a palliative operation, such as gastro-enterostomy, gastrostomy or jejunostomy, may be done to relieve distress and to prolong life for a few months. Seven hundred and thirty-six resections were done at the Mayo clinic with a mortality of 13.7 per cent., 746 explorations, with a mortality of 2.9 per cent. and 612 palliative operations with a mortality of 11.1 per cent. Of patients who survived resection, 38.6 per cent. were free from recurrence for 3 years or more after operation and 26 per cent. for 5 years or more after operation.

DILATATION OF THE STOMACH

Acute Gastrectasis.—The treatment of acute dilatation of the stomach consists in thoroughly washing out the stomach with warm saline solution, even if the patient seems moribund, Elevating the foot of the bed, maintaining the right or left antero-lateral abdominal position, or if the patient's strength permits, the knee-chest position, withholding all food and drink by the mouth, using saline enemas to combat thirst and collapse, and administering subcutaneously such muscle stimulants as physostigmin sulphate— $\frac{1}{50}$ grain (0.0013 gm.), solution of the pit-

uitary body—15 minims (1.0 mil), and strychnin sulphate— $\frac{1}{30}$ grain (0.002 gm.).

Chronic Gastrectasis.—The food should be nutritious, concentrated, and readily digestible, and should be taken in small amounts at somewhat frequent intervals. Liquids are best taken when the stomach is empty and then only in moderate quantities. The importance of thorough mastication must be emphasized. Rest in the recumbent position for an hour after each meal, especially if the patient lies on the right side, favors rapid evacuation of the stomach. A carefully adjusted abdominal bandage affords comfort and gives mechanical support to the stomach. If there is any appreciable stagnation of food lavage should be practised daily, preferably in the early morning or late evening. In mild cases lavage is usually unnecessary. In the non-obstructive form systematic exercise in the open air, hydrotherapy, and abdominal massage, if skillfully applied, are valuable aids. Electricity is of little or no value.

Medicinal treatment must be adapted to the condition with which the motor insufficiency is associated, as, for instance, chronic gastritis, general malnutrition, etc. In uncomplicated or simple atonic dilatation *nux vomica* is useful. It should be given in the form of the tincture, three times a day, and in doses gradually increased to 30 minims (2.0 mils). Antiseptics, such as creosote and betanaphthol, are sometimes of service in lessening the gaseous eructations and the sense of pressure within the stomach arising from fermentation, but, as a rule, more relief is afforded by lavage. The following combination suggested by the late Dr. John H. Musser is often useful:

R. Creosoti..... ℥xii (0.8 mil)
 Spiritus ammoniæ aromatici..... f ℥ii (8.0 mils)
 Spiritus chloroformi..... f ℥i (4.0 mils)
 Sodii bicarbonatis..... ℥ii (8.0 gm.)
 Aquæ menthæ piperitæ..... q. s. ad f ℥iii (90.0 mils)—M.

Sig.—A teaspoonful in a wineglassful of water half an hour after meals and at bedtime.

Constipation is, as a rule, best treated by simple enemas or by suppositories. In some cases, however, Rochelle salt in small doses or mild vegetable cathartics may be employed with advantage.

HEMATEMESIS

In the treatment of hematemesis absolute rest is essential. No food of any kind should be given by the mouth. The foot of the bed should be elevated and an ice-bag applied over the

stomach. A small dose of morphin may be given hypodermically to lessen restlessness and anxiety, although its use has been objected to on the ground that it tends to relax the gastric muscle. The solution of epinephrin (1:1000), in doses of 1 dram (4.0 mils), in a wineglassful of water, every 20 minutes or half hour, may prove useful. Lavage with ice-water or with hot water (120° F.) has apparently been of benefit in some cases.

The passage of the stomach tube is, however, absolutely contraindicated if there is any evidence of hepatic cirrhosis, as the latter often gives rise to extensive varices in the esophageal wall. In persistent bleeding thromboplastin (a hemostatic prepared from brain substance) is worthy of trial. Twenty mils may be taken with a glass of water every two or three hours, or the solution prepared for hypodermic use may be given subcutaneously in doses of 20 mils every 24 hours.

Operation is advisable, however, in recurring profuse hemorrhages, especially if the bleeding is definitely associated with peptic ulcer or splenomegaly (splenectomy).

Collapse following hematemesis will call for elevation of the foot of the bed, hot applications, bandaging of the legs and arms, subcutaneous or intravenous injections of warm saline solution, and above all, if feasible, transfusion of blood.

ACUTE ENTERITIS

Rest in bed, a light diet (boiled milk, arrow root, milk toast, etc.), and the administration of an unirritating purgative, such as castor oil, calomel in fractional doses, or Epsom salt (unless the bowels have been already thoroughly emptied) are all that is required in mild cases. In robust subjects it is even better to withhold all food for twenty-four or thirty-six hours. Severe cases require additional measures. Externally, stupes or sinapisms afford much relief. Internally, the most generally useful remedies are mild astringents, such as bismuth subnitrate or chalk, in fairly large doses (20 gr.—1.3 gm.), and opium, in the form of morphin, codein, or paregoric. Combinations of these drugs with so-called intestinal antiseptics (salol, creosote, etc.) are often efficacious:

R. Codeinæ sulphatis..... gr. ii (0.13 gm.)
 Phenylis salicylatis..... gr. xxiv (1.5 gm.)
 Bismuthi subnitratis..... ʒss (15.0 gm.).—M.

Fiant chartulæ No. xii.

Sig.—One powder every three hours.

R. Phenylis salicylatis..... gr. xxiv (1.5 gm.)
 Tincturæ opii camphoratæ..... f ʒss (15.0 mils)
 Misturæ cretæ..... q. s. ad f ʒiii (90.0 mils).—M.

Sig.—Dessertspoonful every three hours.

Active astringents, such as the preparations of tannin, lead acetate, and silver nitrate, are usually unnecessary, but occasionally if the evacuations are very frequent and copious, they may be given with advantage. A combination such as the following may be prescribed:

℞. Codeinæ sulphatis..... gr. ii (0.13 gm.)
 Tannalbin..... ℥i (4.0 gm.)
 Bismuthi subcarbonatis..... ℥ss (15.0 gm.).—M.
 Fiant chartulæ No. xii.
 Sig.—One powder every three hours.

In the choleraic forms of diarrhea the cramp-like pains are best controlled by subcutaneous injections of morphin (gr. $\frac{1}{12}$ — $\frac{1}{4}$ —0.005–0.016 gm.), or in less severe cases by carminatives with opium by the mouth. Such a combination as the following is often useful:

℞. Spiritus camphoræ..... f ℥ij (8.0 mils)
 Spiritus chloroformi..... f ℥ss (15.0 mils)
 Tincturæ opii camphoratæ..... f ℥vi (22.0 mils)
 Aquæ menthæ piperitæ..... q. s. ad f ℥iii (90.0 mils).—M.
 Sig.—Dessertspoonful every hour or every 2 hours.

When the colon is especially involved, local treatment is advisable. Cleansing enemas of normal salt solution may be given several times a day and followed by injections of warm starch water (one to two ounces). Laudanum (20 min.—1.2 mils) is often added to the starch water, although the opium, of course, has no local action. Tenesmus may be relieved by ice suppositories, inserted at short intervals, or by injections containing cocain (10 min.—0.6 mils—of a 4 per cent. solution).

With the cessation of the diarrhea, increase of food may be allowed, but the return to ordinary diet should always be effected slowly.

CHRONIC ENTERITIS

The cause must be ascertained and removed, if possible. The diet, clothing, habits, occupation, and mode of living of the patient should receive careful attention. The diet is especially important, and the best basis for the appropriate regulation of it, at least as regards particular articles of food, is afforded by systematic examination of the stools after the use of a Schmidt test diet. In all cases the food should be bland, well cooked, and finely divided. Foods that are coarse and leave much residue are inadmissible. Patients with persistent diarrhea sometimes do well on an exclusive milk diet. When the disease is not very

severe and is confined for the most part to the colon, a selected mixed diet may be allowed. The patient's body should be well protected against chilling, and as an additional safeguard a woolen abdominal bandage may be worn with advantage. In severe cases with persistent diarrhea rest in bed for a time may be essential. In milder cases with slight diarrhea or a sluggish condition of the bowels much benefit may be derived from a change of scene and air and carefully graded exercise. To these factors, as well as the strict dietetic regimen to which the patient is subjected, is to be ascribed much of the good that is often obtained from a sojourn at certain health resorts, such as Carlsbad and Vichy in Europe and Hot Springs, Va. and Bedford Springs, Pa., in this country.

As regards medicinal treatment, mild astringents are usually indicated if there is much diarrhea. The most suitable of such remedies are bismuth subnitrate and prepared chalk. If there is marked fermentation small doses of one of the so-called intestinal antiseptics (salol or betanaphthol) may be used as an adjuvant. If the stools are very frequent and watery some preparation of tannin, preferably tannigen or tannalbin, may also be given with advantage. A combination such as the following is sometimes efficacious.

R.	Bismuthi subnitratis.....	℥v (20.0 gm.)
	Phenylis salicylatis.....	℥ss (2.0 gm.)
	Tannalbin.....	℥j-℥iss (4.0-6.0 gm.).—M.
Fiant chartulæ No. xx.		
Sig.—One powder after meals.		

If there is much pain a small amount of codein may be added to this formula. Warm fomentations are useful during acute exacerbations. In the milder cases silver nitrate, combined with extract of opium and administered in keratin-coated pills, is sometimes efficacious. In case of deficient or absent gastric secretion, hydrochloric acid should be given in large doses. In enteritis associated with constipation, saline laxatives are of value. From $\frac{1}{2}$ to 1 teaspoonful of Carlsbad salts may be dissolved in a tumblerful of hot water and taken on an empty stomach early in the morning. Drastic cathartics should be avoided. When the colon is chiefly involved, irrigation, using a double rectal tube, so as not to distend the bowel, is very useful. Hot normal salt solution (110°-120° F.) or a solution of silver nitrate (1:10,000 gradually increased to 1:5000) may be employed for the purpose. At the Mayo clinic good results have been secured in ulcerative colitis from an enema of 3 ounces (90.0 mls) of olive oil and 60 grains (4.0 gm.) of bismuth every night with the patient in the knee-chest position, in order that it may be retained as long as

possible, and 3 to 6 ounces (90.0 to 180.0 mls) of olive oil with 60 to 90 grains (4.0–6.0 gm.) of bismuth daily by the mouth.

DIARRHEAL DISORDERS OF EARLY CHILDHOOD

Much can be done to prevent the occurrence of diarrhea in infants during the summer season. The most important elements in prophylaxis are: the avoidance of weaning in the late spring or summer; the use of suitably modified milk in artificially fed infants; the pasteurization of all milk and reduction of the strength of the mixture during very hot weather; regularity in the hours of feeding; absolute cleanliness of the feeding apparatus and of the mother's or nurse's hands before touching the food; the supply of an abundance of fresh air; daily bathing and on hot days frequent spongings; the avoidance of chilling; and the immediate correction of slight digestive disorders.

At the first sign of intestinal disturbance milk should be withdrawn at once whether the infant is breast-fed or bottle-fed and not resumed for at least 24 hours. It is necessary, however, to give water freely, either as such or in the form of barley-water, rice-water, or strained broth. The return to milk must be made with caution. To remove irritant matter from the bowel, castor oil (2 drams—8.0 mls) or calomel should be given. Irrigation of the colon with normal saline solution once or twice in the twenty-four hours is also useful, especially in ileo-colitis. If the bowel is very irritable the water may be introduced at a temperature of 105° F. In other cases better results are usually secured with cool water (80°–90° F.). With persistent fever and frequent stools, it may be necessary to repeat the laxative. In most cases it is necessary to follow the laxative with a mild astringent, such as bismuth subcarbonate or chalk. The former is usually preferable and may be given in doses of 10 grains (0.65 gm.), suspended in cinnamon water or peppermint water, at two-hour intervals. A more active astringent, such as tannalbin (1–2 grains—0.065–0.13 gm.), may be given in addition to the bismuth or chalk if the discharges are very profuse and watery, although it is rarely required.

Opium is often of value, but great caution must be exercised in its use. It is indicated when the diarrhea persists despite the thorough unloading of the bowel and the use of mild astringents, and when pain or tenesmus is pronounced. Paregoric in doses of 5 to 10 minims (0.3–0.6 mil), every 2 to 4 hours, is, as a rule, the best preparation. It may be added to the bismuth, but owing to the necessity of a frequent change of dosage, it is better not combined with the astringent in the same prescription. If

the stomach is unretentive, tincture of opium (2-3 minims—0.12-0.2 mil) may be given by enema. The starch enema (1-2 ounces—30.0-60.0 mls) is a time-honored remedy for severe tenesmus. It is made by mixing into a smooth paste a dram (4.0 gm.) of starch with a little cold water and then adding boiling water until a mucilage is formed. Laudanum is often added to starch mucilage, but its action is, of course, purely central. The application of hot stupes or compresses to the abdomen frequently renders the use of opium unnecessary. In persistent colitis injections of silver nitrate (1:1000) are sometimes useful.

Stimulants are not rarely required. The best are tincture of nux vomica in doses of 1 minim (0.06 mil), equal to $\frac{1}{400}$ grain (0.00016 gm.) of strychnin, for an infant of 1 year; caffein-sodium benzoate, $\frac{1}{4}$ - $\frac{1}{2}$ grain (0.016-0.03 gm.), by mouth or subcutaneously; camphor, $\frac{1}{2}$ grain (0.03 gm.) in oil, subcutaneously; and brandy or whisky, 5 to 15 minims (0.3-1.0 mil) well diluted with sweetened water, by the mouth.

Temporary removal to the seashore or mountains is often of the greatest benefit, when the disease loses its acute character but tends to persist.

In **cholera infantum** the stomach should be washed out with cool water and the bowel irrigated. As a rule, however, neither process should be repeated. At first nothing should be given by the mouth but cold water and brandy or whisky. If the stomach is wholly unretentive stimulants should be given hypodermically. If the temperature is low hot baths (105° F.), lasting 5 minutes, may be given at frequent intervals. On the other hand if the temperature is high cool packs (85° F.) should be substituted. Colonic irrigation with cool water (90°-80° F.) also aids in reducing pyrexia.

Persistent vomiting and purging are best treated by morphin and atropin hypodermically. For a child of 1 year $\frac{1}{100}$ grain (0.00065 gm.) of morphin may be given with $\frac{1}{600}$ grain (0.0001 gm.) of atropin, and repeated as required, but not more frequently than once in 3 hours. In desperate cases normal salt solution should be used subcutaneously, from 2 to 3 ounces (30.0-90.0 mls) being injected 3 or 4 times a day.

After vomiting has ceased, barley-water, albumin-water, or fresh beef-juice may be given by the mouth. Milk feeding should always be resumed very cautiously.

ACUTE APPENDICITIS

As no one can foretell the outcome of an attack of appendicitis once it has begun, as the mortality with early operation is

much lower than with any other form of treatment, operation should always be recommended as soon as the diagnosis is made, unless the services of an operator with the requisite skill cannot be secured, unless proper facilities for operating are not at hand, or unless the patient has some additional ailment that would make medical or expectant treatment seem the more safe procedure. On the whole, the best results are secured by a close cooperation of internist and surgeon. The chief aim of medical treatment is to quiet peristalsis and thus hinder the spread of the infection. From the first appearance of suggestive symptoms the patient should be at complete rest in bed, with an ice-bag over the abdomen to relieve pain. No food whatever and no water or ice should be given by the mouth. Enteroclysis by the drop method may be employed, however, to relieve thirst. Aperients, even the mildest, are absolutely contraindicated. Nausea or vomiting is best controlled by washing out the stomach. Morphin as an analgesic is undesirable, as it tends to mask the symptoms. It may be given, of course, in accordance with the indications, when operation is refused or for some reason cannot be recommended. Otherwise it should be given only in minimal doses after the diagnosis has been definitely made, or pending an operation.

If the patient is not seen within the first forty-eight hours and already presents the symptoms of diffuse peritoneal infection and toxemia—frequent pulse (130–140), high temperature (102°–103° F.) pinched features, cyanosis, extreme abdominal distention, diffuse tenderness and rigidity, intestinal paresis, etc., it is probably better not to open the abdomen at once, but to wait for localization of the process, following in the meantime the plan of treatment suggested by Ochsner to control peristalsis and favor limitation of the infection. Some surgeons, however, believe that more lives are saved by making a simple incision, thus relieving the tension and affording exit to the infected exudation. Briefly stated, Ochsner's treatment consists in maintaining the Fowler position, washing out the stomach, withholding food, water, and all medicines by the mouth, applying heat or cold to the abdomen, and giving saline solution freely by the rectum, and, if necessary, also by subcutaneous injection.

MUCOUS COLITIS OR MUCOUS COLIC

Dietetic measures play an important part in the treatment, but no one kind of diet is suitable for all cases and changes must frequently be made to meet special indications. Generally speaking, the diet should be liberal, solid rather than liquid, and

unirritating. The diet of coarse foods, recommended by von Noorden, has not had many advocates in this country, but it may prove serviceable if the attending constipation is atonic rather than spastic. All writers are agreed that the establishment of a normal action of the bowels is absolutely essential to the achievement of a permanent cure. For this purpose, in addition to dietetic regulations, it is usually necessary to employ laxatives or intestinal irrigation, as well as the physical measures described under Habitual Constipation, and to continue them for several months after apparent recovery. Castor oil, if well received by the stomach, is one of the best laxatives. It should be given in doses of from $\frac{1}{2}$ to 1 ounce (15.0–30.0 mls) in the early morning. In some cases liquid petrolatum may be substituted for the castor oil with advantage. In other cases cascara sagrada or a combination of this remedy with agar acts satisfactorily. Salines are less efficacious, as a rule, and drastic purgatives are contraindicated. Colon-irrigation, several times a week with normal saline solution (100° F.) or a solution of sodium bicarbonate (a teaspoonful to a liter of water), if practised regularly, often affords much relief. For many years at Plombières and Chatel-Guyon in France and at Harrowgate in England treatment by intestinal irrigation has been carried out with excellent results. Occasionally, lavage of the colon seems to increase the secretion of mucus. In such cases enemas of bland oil often prove effective and may be given as follows: 200 to 500 mls of slightly warmed linseed, sesame, or olive oil or liquid petrolatum are injected at first every night, then, after three weeks every other night, and later with decreasing frequency. The injections should be given slowly through a soft rubber tube, the patient remaining on the left side for ten minutes. If possible, the oil should be retained overnight. Sometimes an enema of olive oil, bismuth subcarbonate and tincture of belladonna gives better results than one of oil alone. The following proportions may be used:

Rx. Olive oil.....	8 ounces (235 mls)
Bismuth subcarbonate.....	60 grains (4.0 gm.)
Tincture of belladonna.....	5 minims (0.3 mls)

Measures to improve the patient's general health are almost always required. A modified or partial Weir Mitchell rest cure is of much benefit in some cases; in others systematic exercise in the open air, provided it is not too fatiguing, yields better results. A change of scene is often helpful. Hydrotherapy is of considerable value. Tonics, such as iron, arsenic, nux vomica, are useful as occasion may demand. In some instances the

bromids for a short time, either alone or in association with belladonna, seem to be of service. Any associated abdominal condition, such as appendicitis, adhesions, cholecystitis, etc., should receive appropriate treatment, but radical measures should be avoided unless the indications are very definite. If visceroptosis is a prominent feature, a straight front supporting corset or Rose's adhesive plaster belt may accomplish much good. Finally, in very severe and otherwise intractable cases surgical measures that will facilitate irrigation of the entire colon, such as cecostomy, or tend to remove intestinal stasis, such as partial colectomy, may have to be considered.

In the attacks of severe colic, rest in bed, the application of heat to the abdomen, the administration of a full dose of castor oil and of belladonna, with codein, if necessary, colonic irrigation with a solution of sodium bicarbonate or the use of a warm oil enema are the measures that afford the most relief.

CHRONIC CONSTIPATION

Although certain remedial measures are applicable to many cases of constipation, no method of treatment can be entirely satisfactory that does not take into consideration the causal factor and effect its removal. In constipation due to atony of the bowel foods that yield much undigested residue are indicated, provided, of course, that they do not disturb digestion. Thus, vegetables rich in cellulose, such as lettuce, celery, spinach, string beans and tomatoes, and farinaceous foods containing the hulls of grain, such as graham and whole wheat bread, and oatmeal gruel or crackers, should be given. Fruits and nuts, if well borne by the stomach, are especially useful. In mild cases a few English walnuts after dinner or an orange before breakfast may supply the necessary stimulus to peristalsis. Fats and oils form soaps, which are laxative and, if well received by the stomach, may have a very useful effect, particularly if the patient's general nutrition is poor. While a certain amount of water is necessary, an excess is more likely to be diuretic than laxative, unless it is held in the bowel by a salt difficult of absorption (Epsom or Rochelle salt) or by some inert substance which readily swells in water (agar-agar). In a small percentage of cases even half a dram (2.0 gm.) of Epsom salt taken in a glass of water before breakfast is effective. Agar-agar (2-6 teaspoonfuls daily) may be served in broths, gruels, or cooked fruits, or may be taken dry and washed down with fluid.

The cultivation of regular habits in regard to defecation is of prime importance and therefore the patient should be instructed

to make a determined effort to have a bowel movement once daily, always at the same hour, preferably in the morning after breakfast, even if there is no desire at the time or whether a result is obtained or not. At first the effort will have to be supplemented by the use of a glycerin or soap suppository, or a small enema of normal saline solution, but gradually these aids should be withdrawn.

For patients with relaxed and weakened abdominal muscles systematic exercise in the open air, if possible, or indoors, if necessary, is indispensable. Massage, if correctly given over a long period of time, is also of service. In mild cases self-massage may be practised by kneading the abdominal muscles in the direction of the colon or by rolling over the abdomen in the same direction a cannon-ball (3 or 4 pounds) covered with chamois-skin. Hydrotherapy, especially in the form of cold abdominal compresses or the abdominal douche with hot and cold water alternately (so-called Scotch douche) is a valuable addition to physical exercise. Patients with visceroptosis or a large pendulous abdominal wall should wear a suitable belt, and this should be applied before rising in the morning and not removed until bedtime.

When the stasis is mainly in the pelvic colon or rectum (dyschezia) enemas of plain water, soap and water, or normal saline solution are preferable to cathartics by the mouth. Injections of warm black coffee are sometimes very effective. Glycerin (a teaspoonful) is also efficacious. For occasional use, when it is necessary to empty the bowel quickly, the following compound enema will be found efficient:

R. Magnesii sulphatis.....	℥ii (60.0 gm.)
Olei terebinthinæ.....	f℥ss (15.0 mls)
Glycerini.....	f℥i (30.0 mls)
Aquæ.....	q. s. ad f℥iv (120.0 mls)

In the milder cases of constipation suppositories of glycerin, soap or gluten may suffice. Neither enemas nor suppositories should be used continuously for long periods, for in time they render the bowel less responsive to natural stimuli. If there is fecal impaction, if hard scybala occur in the stools, or if there is abnormal secretion of mucus, injections of warm cottonseed oil (100° F.) may often be used with advantage. The oil is best given at bedtime and allowed to remain in the bowel over night. It should be introduced slowly while the patient is on the back with the hips raised. From 4 to 6 ounces (120.0–180.0 mls) may be

injected every two or three days. If necessary the injection of oil may be followed by one of plain water. Hard fecal masses in the rectum may also be softened by enemas containing ox-gall (2 drams—8.0 gm.) to the pint (0.5 L.) of water. Very hard collections must sometimes be broken up by the gloved finger or a blunt instrument before they can be evacuated by enemas.

Irrigation of the colon at intervals of two or three days sometimes yields very good results in the cases of stasis in which obscure cerebral symptoms are present or in which hard, foul-smelling masses are occasionally passed. The rectum and sigmoid should first be emptied by an enema and then 2 or 3 pints of warm normal salt solution should be allowed to flow in and out of the bowel through a soft rubber colon tube while the patient lies on the left side, with the knees drawn up, and with the abdomen as relaxed as possible. The reservoir should be held at a height of about 2 feet and the tube should be introduced for a distance of 6 inches, backward and forward movements being constantly made so as to permit the escape of any gas that may be present.

Dietetic and physical treatment will not cure all cases of constipation and the administration of drugs often becomes a necessity. For habitual use the anthracene cathartics—cascara, aloes, rhubarb, senna, and phenolphthalein—are usually chosen. A sufficient dose should be employed to secure a satisfactory movement, but it is important to avoid active purgation. As a rule, a combination of two or three drugs is more effective than a single drug. *Nux vomica* or *physostigma* is often added to the combination to enhance its stimulating effect, and *belladonna* to prevent griping. Ordinarily, vegetable laxatives cause less inconvenience when taken at bedtime or after the evening meal. Sometimes, however, better results are obtained by giving small doses after each meal. Such combinations as the following often prove satisfactory:

℞. Extracti cascarae sagradae..... gr. xlviii (3.1 gm.)

Aloini

Extracti nucis vomicae..... āā gr. iv (0.25 gm.)

Extracti belladonnae..... gr. iii (0.2 gm.)

Misce et fiant pilulae No. xxiv.

Sig.—One pill at bedtime.

℞. Phenolphthaleini..... gr. xx-xxx (1.3-2.0 gm.)

Extracti nucis vomicae

Extracti physostigmatis..... āā gr. iii (0.2 gm.)

Extracti belladonnae..... gr. iv (0.25 gm.)—M.

Fiant pilulae No. xx.

Sig.—One pill at night or night and morning.

R.	Extracti cascarae sagradae.....	gr. xl (2.5 gm.)
	Resinae podophylli.....	gr. iii (0.2 gm.)
	Extracti colocynthis compositi....	gr. xxx (2.0 gm.)
	Extracti physostigmatis.....	gr. iv (0.25 gm.)
	Extracti hyoscyami.....	gr. x (0.65 gm.)

Misce et fiant pilulae No. xx.

Sig.—One pill night and morning.

In some cases of constipation, especially if gout, diabetes or chronic gastric catarrh is also present, salines are preferable to vegetable cathartics. One of the natural mineral waters, such as Hunyadi, Apenta, Bedford or Saratoga may be employed, although equally good results may be obtained from 1 or 2 drams (4.0–8.0 gm.) of Rochelle salt, magnesium sulphate, or sodium phosphate, taken before breakfast or at night in a glass of hot or cold water. In conjunction with enemas and careful abdominal manipulation, salines in small doses at short intervals are also the cathartics of choice in fecal impaction. In the cases in which gastric hyperacidity accompanies constipation magnesium oxide is especially valuable. Castor oil and calomel are not suitable for continuous use, but are often very serviceable in acute exacerbations. When the stools are dry, or the constipation is the result of enterospasm or of partial obstruction, or is accompanied by mucous colitis, pure liquid petrolatum is frequently of value. From $\frac{1}{2}$ to 1 ounce (15.0–30.0 mls), with cold water or orangeade, should be taken at night or two or three times a day between meals, that is when the stomach is empty. It is sometimes necessary to add a small amount of cascara to secure the best results.

In spastic constipation general massage is sometimes useful, but all local stimulation must be forbidden. Periods of absolute rest are often imperative. Warm abdominal compresses are efficacious, especially when there is much colicky pain. Harsh, irritant foods are harmful. Injections of a few ounces of warm oil every night or every other night are of great value. By the mouth, liquid petrolatum and agar-agar are worthy of trial. Atropin, beginning with $\frac{1}{100}$ of a grain (0.00065 gm.) twice a day, and gradually increasing the dose until physiologic effects are produced, is sometimes successful. A glass of hot water night and morning also tends to relax the spasm of the bowel. From time to time moderate doses of castor oil to which a few drops of laudanum have been added may often be used with advantage. Dilatation of the sphincter has been tried with varying success.

Surgical Treatment.—In certain well chosen cases of chronic constipation good results may sometimes be obtained by surgical

treatment. The most important measures are suspension of the colon, partial or complete colectomy, and various short circuiting operations. The patients most likely to be benefited by surgical intervention are those in whom there is definite evidence of partial obstruction and who have become disabled by the condition despite protracted and varied medical treatment. Such serious measures, however, cannot be undertaken without some risk even by the most skillful and are certainly inadvisable for congenital cases presenting signs of faulty development outside of the intestinal tract or for the relief of nervous symptoms in cases of simple constipation, no matter how severe this may be.

VISCEROPTOSIS

(Gastroptosis, Enteroptosis, Nephroptosis)

The chief indications are to elevate the prolapsed organs and to keep them in place by providing adequate support, to relieve any local disturbances that may occur in the affected organs, to correct any existing postural abnormalities and to improve the general nutrition. To keep the prolapsed organ in its normal position mechanical supports which make pressure from below upward and backward are often of value. The support may consist (1) of strips of adhesive (zinc oxid) plaster, about 3 inches wide, passed obliquely around the abdomen from the region of the symphysis upward and backward, crossing in front and back; (2) of a specially designed abdominal binder; or (3) of the so-called straight-front corset. It is important that the binder or corset should be applied while the patient is in the supine posture with the thighs flexed, and removed only when he is again recumbent. Neither binder nor corset is likely to be of service if the abdomen is scaphoid or the ptosis is extreme. In nephroptosis it may be necessary to use a suitable pad in addition to the other means of support. Rest in the horizontal position, particularly after each meal, often affords much relief. In order to correct postural abnormalities and to improve the tone of the abdominal muscles special gymnastic exercises are unquestionably of much benefit. Constriction of the lower portion of the thorax by tight clothing of any kind must be forbidden. Improvement in the general nutrition is best secured by dietetic and hygienic measures. Liberal feeding is usually required, but in all cases the diet should be carefully adapted to the digestive capacity of the patient. Hydrotherapy is often very useful. Tonics, especially strychnin, are sometimes indi-

cated. Neurasthenia will require the general measures advocated in the section dealing with that condition. The treatment of constipation and other local disturbances is the same as for like conditions in normally placed organs.

Surgical Treatment.—In carefully selected cases appropriate surgical treatment—suturing the prolapsed organ to an adjacent structure, shortening of its supporting ligaments, etc.—may afford complete relief, but frequently the results are more or less unsatisfactory. Relapse is common and not rarely the operation is followed by the formation of troublesome adhesions. Certainly, surgical treatment should not be recommended unless there are definite local disturbances which cause persistent discomfort or serious impairment of nutrition and which resist all other measures. Operation undertaken for the relief of neurasthenic symptoms or vague disturbances referable to a number of organs is much more likely to do harm than good.

CATARRHAL HEPATITIS; CATARRHAL JAUNDICE

The treatment of catarrhal jaundice is, for the most part, that of acute gastrointestinal catarrh. Rest in bed and restriction of the diet to milk with lime-water or Vichy water, or to light broth are indicated until the digestive disturbance has subsided. In the presence of nausea and vomiting abstinence from food for 24 or 36 hours is advisable. Even after the disappearance of the gastric irritation the nourishment should be simple and in moderate quantity. The bowels should be kept open by small doses of calomel, followed by a saline cathartic or by sodium phosphate, preferably in hot water. Bismuth subcarbonate or silver nitrate ($\frac{1}{4}$ grain—0.016 gm., in pill, three times a day) is sometimes of service. Hexamethylenamin has been recommended as a biliary antiseptic but it is valueless. Ammonium chlorid, in doses of 10 grains (0.6 gm.) three times a day, lessens the viscosity of mucous secretion and, in consequence, may prove effective. Hot, wet compresses over the upper part of the abdomen seem to be useful. In refractory cases the direct introduction of a 25 per cent. solution of magnesium sulphate into the duodenum through a duodenal tube, once a day, has been found efficacious.*

* Meltzer showed that a 25 per cent. solution of magnesium sulphate, when introduced directly into the duodenum, relaxes the bile duct and permits of a free flow of bile from the gall-bladder to the duodenum. Lyon has reported excellent results from the use of this solution in obtaining duodenal contents for diagnostic purposes and also as a means of treating inflammatory conditions of the biliary tract. The procedure is carried out

Chronic catarrhal jaundice requires similar treatment. Rest, a light, simple diet and the use of mild mercurial and saline aperients are indicated. Water drinking between meals should be encouraged. Alkaline mineral waters (Vichy, Vals, Hathorne, Vittel) may be used. Daily irrigation of the colon with cold water (1-2 liters) is of service, but in some cases it is less effective than the administration of a solution of magnesium sulphate through the duodenal tube. Pruritus may be relieved by a lotion of phenol, 2 drams (8.0 gm.) to the pint (0.5 L.), or of resorcin:

R̄.	Resorcinolis.....	℥iss (6.0 gm.)
	Sodii chloridi.....	℥i (4.0 gm.)
	Glycerini.....	f℥i (30.0 mls)
	Liquoris calcis.....	q. s. ad Oj (0.5 L.)

CHRONIC CHOLECYSTITIS AND CHOLELITHIASIS

(Gall-stones)

An important object of treatment is to promote a free flow of unirritating bile, and to accomplish this dietetic and hygienic regulations demand the first consideration. The diet should be mixed, bland, easily digestible, and generous rather than meagre. Strong soups, heavy gravies, potted and preserved meats, high game, greasy pastry, overripe cheese, much sweets, highly seasoned dishes and alcoholic beverages of all kinds should be avoided. The food must be thoroughly masticated and should be taken neither too hot nor too cold. In some cases, if the gastric digestion is well maintained, it is advantageous to give the food in smaller quantities and at comparatively short intervals. A light meal at bedtime has been specially recommended by Kehr. Frequent feeding may prove harmful, however, if there is atony of the stomach with impairment of gastric motility. An important point is the supply of sufficient water to dilute the body fluids and to remove from the alimentary canal irritating products of digestion. A glass of hot Carlsbad water, or if this is not well borne, of cool plain water, may be taken between meals and at bedtime, and before or after rising. To increase still further the supply of fluid without interfering with digestion a rectal injection of two quarts or more of cool water every few days is often beneficial. Exercise in the open air, regulated according to the

in the fasting state. After the patient's stomach has been thoroughly rinsed and he has been placed on his right side with the hips slightly elevated, he is given a glass of water to drink, and then by *slow* swallowing the tube is allowed to enter the duodenum. When the latter is reached (15 to 45 minutes) 50 mls of a sterile 25 per cent. solution of magnesium sulphate are introduced.

patient's needs and habits, unquestionably has a salutary effect, provided of course, there are no acute symptoms. Systematic deep breathing is also useful in overcoming the tendency to portal and biliary stasis. Constriction of the upper part of the abdomen by corsets or other articles of dress must be avoided. Freedom from worry and mental strain rarely fails to afford some relief.

Digestive disturbances and constipation should receive appropriate treatment. If necessary, laxatives should be used. Sodium phosphate, Carlsbad salt, or Rochelle salt may be added to the water which is drunk before breakfast and between meals. The natural mineral waters probably have no special advantages, although those of Carlsbad and Vittel have a high reputation. An occasional course of calomel, in fractional doses, is often useful. Among special remedies, sodium succinate—5–10 grains (0.3–0.6 gm.) after meals—is worthy of trial. Hexamethylenamin, up to a total of 30 grains (2.0 gm.) a day, has been recommended for its antiseptic properties, but it is doubtful whether it yields enough formaldehyd in the biliary passages to be effective. Sodium glycocholate—5 grains (0.3 gm.) after meals—has a cholagogue action, and may be of value in some cases. The introduction of magnesium sulphate by tube into the duodenum, as recommended by Lyon (see p. 639), may aid in draining the gall-bladder. If the patient's circumstances will permit a course of treatment at Carlsbad, Vittel, Contrexville, or Vichy in Europe, or at Bedford or Las Vegas Hot Springs in America may be recommended with some degree of confidence. An extended visit at one of these resorts is often followed by marked improvement and occasionally by permanent relief. The benefit probably depends as much upon change of air and scene, genial surroundings, freedom from worry, and regular hours as upon the action of the waters themselves. If no benefit accrues from medical treatment after a thorough trial surgical aid should be invoked without further delay, otherwise serious complications are likely to supervene. The mortality of operation in simple cases and in expert hands is less than 2 per cent.

The medical treatment of *cholelithiasis* is essentially that of cholecystitis, for chronic catarrh of the gall-bladder is the chief cause of the formation of gall-stones, and when these are already present, a reactivation of the inflammatory process is mainly responsible for mobilization of the stones and the occurrence of colicky pains. Attempts to promote the solution of gall-stones or to effect their expulsion by means of drugs have met with very little, if any, success, and therefore our main reliance must be on measures which tend to allay inflammation in the biliary tract

and keep the stones quiescent. These measures have already been dealt with in discussing the treatment of chronic cholecystitis.

Hepatic Colic.—If the pain is severe it will be necessary to give morphin with atropin at frequent intervals. As the opium habit is readily formed in these cases it need scarcely be added that great caution should be exercised in the use of the drug. Agonizing pain often yields to a few whiffs of chloroform. In the milder but more persistent attacks a few doses of antipyrin, 5 to 7 grains (0.3–0.5 gm.) in copious draughts of hot water may suffice. The external application of heat is very useful. Hot poultices or fomentations may be applied to the region of the liver, or if circumstances permit, the patient may be kept in a hot bath. Exceptionally, an ice-bag affords more relief than a hot application. If vomiting is excessive, carbonated water, cracked ice, small quantities of champagne, or cerium oxalate may be given. In threatened collapse diffusible stimulants are needed.

Surgical Treatment.—Surgical intervention is indicated—(1) when despite medical treatment attacks of colic occur so frequently and are of such severity as to cause disability or make addiction to morphin a likelihood; (2) if, as a result of chronic cholecystitis or of pericholecystic adhesions, there is intractable indigestion with non-colic pains; (3) in persistent enlargement of the gall-bladder, even if pain and jaundice are absent; (4) in obstruction of the common bile-duct, if the symptoms persist after two, or at most three, weeks of rest, dieting and local applications of heat; and (5) if there are evidences of pancreatitis, acute or chronic. In the hands of skillful surgeons the mortality of operations on the gall-bladder in uncomplicated cases is very low, certainly less than 2 per cent. and the all-round mortality, excluding cases of malignant disease, is probably not more than 7 or 8 per cent. Complete and permanent relief may be confidently expected after operation in a very large proportion of the early cases. Cholecystectomy gives much greater prospect of permanent cure than cholecystotomy. C. H. Mayo reports that in 2460 cases in which cholecystectomy was performed for cholecystitis with or without stones the mortality was only 1.8 per cent. Recurrence in the sense of the actual formation of new stones is rare even after cholecystotomy, subsequent disturbances usually being the result of a persisting cholecystitis, of calculi that have been overlooked during the operation, or of pericholecystic adhesions. If jaundice has been present for a long time it is advisable to administer blood-serum (50 to 150 mls) subcutaneously and calcium lactate by the mouth with the view of reducing the coagulation time of the blood and preventing capillary oozing.

CIRRHOSIS OF THE LIVER

Atrophic or Portal Cirrhosis.—In the hope that something may be done to arrest the progress of the disease, alcohol, all stimulating and highly seasoned foods, and all foods likely to increase the digestive disturbances, such as articles rich in fat or sugar, should be prohibited. Eggs, tender meat, and well-cooked vegetables and cereals may usually be allowed, but in some cases an exclusive milk diet for the first three or four weeks is advisable. Often as much depends upon temperance in eating as upon the choice or rejection of certain foods. If feasible spa treatment may be of service by affording the patient an opportunity to change his diet and mode of life and by teaching him how he must live thereafter. Measures which promote the action of the skin and kidneys should not be neglected. If there is a suspicion that syphilis has played any part in the production of the disease, such drugs as arsphenamin, mercury and iodids, should be given a thorough trial, although it must be recognized that even if the influence of syphilis is unquestioned, no drug can materially affect the cirrhotic process itself. The portal system is best depleted by saline aperients and the occasional use of a mild mercurial. Mineral waters, such as those of Vittel, Carlsbad, and Hunyadi János, taken hot an hour before meals, sometimes have a good effect.

Ascites, if not speedily relieved by purgatives (salines, compound jalap powder, or blue mass), diuretics (theobromin, theocin, caffein, or digitalis), the Baillie or Niemeyer pill (digitalis, squill and blue mass), and a dry diet, should be tapped. The operation (*paracentesis abdominis*), if done with reasonable care and under aseptic precautions is virtually devoid of danger. Occasionally, after a number of tappings the fluid does not return for a long period—perhaps several months or even years—generally, however, the abdomen quickly refills and withdrawal of the fluid at short intervals is necessary. The operation is performed as follows: The bladder having been emptied and the skin of the abdomen carefully cleansed, the patient is placed in a semirecumbent position near the edge of the bed. The puncture is usually made in the median line midway between the symphysis pubis and the navel, but if owing to adhesions or other causes the fluid cannot be withdrawn in this situation, it may be made on the left side midway on a line between the symphysis and the anterior-superior spine of the ileum. The area selected for the puncture may be anesthetized, if necessary, by means of a block of ice sprinkled with salt or by a spray of ethyl chlorid. The trocar (about $\frac{1}{8}$ inch in diameter) is introduced into the abdominal

cavity with a quick thrust and the escaping fluid is then conducted through a rubber tube, attached to the cannula, into a pail placed by the side of the patient's bed. If the flow becomes interrupted, it may often be reestablished by changing the direction of the cannula or passing into it an aseptic probe. While the fluid is escaping a many-tailed binder should be adjusted to the abdomen and gradually tightened. The binder gives support to the relaxed abdominal wall, and tends to prevent syncope, tympanites and hematemesis. It should be kept on two or three days. After the fluid has ceased to flow, the cannula is removed, and the wound sealed with a sterile pad and a few strips of adhesive plaster.

Hypertrophic Biliary Cirrhosis (Hanot's Cirrhosis).—The treatment is largely symptomatic. Hexamethylenamin has been recommended, but it is of doubtful value. Calomel, in doses of $\frac{1}{8}$ to $\frac{1}{4}$ grain (0.008–0.016 gm.), every three or four hours, periodically, for three or four days, has also been extolled (Sacharjin, Goluboff). Drainage of the gall-bladder and biliary ducts is said to have resulted in improvement, and in a few cases of supposed Hanot's cirrhosis splenectomy has been followed by a cure.

Obstructive Biliary Cirrhosis.—The treatment is mainly that of the causative condition. Removal of gall-stones and drainage of the bile-ducts, however, are not always curative. W. J. Mayo has observed marked improvement from splenectomy in a number of long-standing cases with enlargement of the spleen.

ACUTE AND CHRONIC PANCREATITIS

Acute Pancreatitis.—The treatment is purely surgical. Operation consisting of exposure of the pancreas and free drainage should be performed as soon as possible after the onset of the disease. Fortunately, it is not necessary that the diagnosis should be made with absolute certainty before the abdomen is opened since the conditions most likely to be confused with acute pancreatitis also demand immediate surgical treatment.

Chronic (Interlobular) Pancreatitis.—The treatment of chronic interlobular pancreatitis should aim at the cause, whether this be gall-stones, duodenal ulcer or catarrh, or syphilis. A thorough study of the digestive processes and the adaptation of the diet to existing deficiencies will often lead to improvement. Preparations made from the pancreas are sometimes useful. If after a fair trial of medical treatment the symptoms still persist, the question of draining the biliary tract, and through

this outlet also the pancreatic ducts, should be of seriously considered. Even when there is no definite evidence of cholelithiasis, cholecystectomy, cholecystostomy, or choledochoduodenostomy may prove effective in arresting the process.

DISEASES OF THE RESPIRATORY TRACT

CORYZA

(Acute Catarrhal Rhinitis)

If the patient is seen at the outset and is willing to remain indoors for twenty-four hours, a hot foot-bath with a full dose of Dover's powder, followed in the morning by a saline aperient, often yields good results. Frequently such combinations as the following will afford relief:

℞. Codeinæ sulphatis..... gr. iii (0.2 gm.)
 Ammonii chloridi
 Terpini hydratis..... āā ʒiss (6.0 gm.)
 Extracti hyoseyami..... gr. xii (0.8 gm.).—M.

Pone in capsulas No. xxiv.

Sig.—One capsule after meals and at bedtime.

℞. Codeinæ sulphatis..... gr. ii (0.13 gm.)
 Ammonii carbonatis..... gr. xxx (2.0 gm.)
 Extracti belladonnæ..... gr. i (0.065 gm.)
 Pulveris camphoræ..... gr. xv (1.0 gm.)
 Acetphenetidini..... gr. xxx (2.0 gm.).—M.

Pone in capsulas No. xv.

Sig.—One every three hours.

Cleansing of the nares with warm, well-diluted Dobell's solution usually lessens the local discomfort, especially if it is followed by an oily application as a protective. The following combination may be used:

℞. Mentholis..... gr. iii (0.2 gm.)
 Petrolati liquidi..... f ʒj (30.0 mls).—M.

Inhalations of menthol are also useful. When there are recurrent attacks of acute rhinitis the indications are to procure the best hygienic conditions, to improve the patient's general health, and to remove any local obstruction that may exist in the nasal passages. The use of mixed stock vaccines sometimes yields good results, although it fails completely in at least one-half of the cases.

EPISTAXIS

In certain conditions nose-bleed may prove beneficial by relieving undue tension in the vascular system. There is no doubt that in diseases of the mitral valves moderate epistaxis at times affords considerable relief. Again, it is quite possible that spontaneous nasal hemorrhage sometimes averts cerebral apoplexy in middle-aged persons with high bloodpressure. Sometimes epistaxis does not cease spontaneously, but becomes excessive. Under these circumstances active measures must be adopted. The patient should be kept quiet, with the head and shoulders slightly elevated, and should be directed to breathe through the mouth. Ice may be applied over the nose or nape of the neck, and one or both hands held above the head. Injections of cold diluted vinegar or insufflations of tannin or of powdered alum may often be used with advantage. The most efficient local remedy, however, is epinephrin (1 : 1000), applied on a cotton tampon. Powdered coagulose or coagulen, on a pledget of cotton, is recommended in hemorrhagic diseases. If the blood is found to issue from a small ulcer, the Paquelin cautery (brought to a dull red heat), chromic acid, fused on the end of a probe, or silver nitrate may be applied. If the bleeding resists these measures the nares should be plugged. Internal remedies are not often of service, although calcium lactate, by the mouth, may prove effective in bleeding associated with jaundice and fresh blood-serum (30 mls daily), intravenously or subcutaneously, in that due to hemophilia or purpura hemorrhagica. Thromboplastin solution (20 mls subcutaneously every 24 hours) or coagulose (the contents of an ampule) may also be tried when the blood seems to lack coagulability.

In the after-treatment the indications are to overcome anemia, if this is pronounced, and to remove, if possible, any underlying condition that may be a cause of epistaxis.

ACUTE LARYNGITIS

In severe cases the patient should be confined to bed, and the temperature of the room should be kept uniformly at 70° F. The use of the voice should be avoided. A hot foot-bath is sometimes of service. Cold compresses externally often afford much relief. Inhalations of steam impregnated with compound tincture of benzoin or oil of eucalyptus are useful. At the onset it is advisable to administer a mild aperient. Sedative expectorants, such as potassium citrate and ipecac, may be given with paregoric or codein when the cough is severe. A combination such as the following will often meet the indications:

- R. Tincturæ aconiti..... f 3i (4.0 mils)
 Syrupi ipecacuanhæ..... f 3iv (15.0 mils)
 Tincturæ opii camphoratæ..... f 3ss (15.0 mils)
 Liquoris potassii citratis.... q. s. ad f 3vi (180.0 mils).—M.
 Sig.—A tablespoonful every four hours.

Spasmodic Croup.—A sponge wrung out of hot water may be applied over the larynx or the child may be placed in a hot bath. If these simple measures fail an emetic (1 to 2 teaspoonfuls of syrup of ipecac) will usually afford relief. A moist atmosphere tends to prevent a recurrence of the attacks. In the intervals the treatment is that of simple catarrhal laryngitis. A combination of a sedative expectorant, such as ipecac or potassium citrate, with an antispasmodic, such as potassium bromid, antipyrin or belladonna, is often useful.

- R. Tinctura aconiti..... ℥xvi (1.0 mil)
 Syrupi ipecacuanhæ..... f 3i (4.0 mils)
 Potassii bromidi..... 3i (4.0 gm.)
 Syrupi limonis..... f 3ss (15.0 mils)
 Liquoris potassii citratis.... q. s. ad f 3ii (60.0 mils).—M.
 Sig.—A teaspoonful every 2 or 3 hours for a child of 3 years.

In older children the application of cold compresses to the neck has a favorable effect.

EDEMA OF THE LARYNX

Mild attacks sometimes yield to the application of an ice-bag to the neck, the sucking of ice, external depletion by leeches, the use of astringent sprays (epinephrin, alum, tannic acid) and the administration of saline purges. If the symptoms are urgent the edematous parts should be scarified under cocain anesthesia, and if this fails, tracheotomy should be performed at once. Intubation rarely affords relief unless the obstruction is infraglottic.

ACUTE BRONCHITIS

If the patient be weak or old he should be confined to his room or even to bed. It is advisable to keep the atmosphere of the room moist and at a temperature not above 70° F. In the early stage a hot foot-bath at bed time, with a Dover's powder and a hot drink, often appears to influence favorably the course of the disease. The food should be simple and readily digestible, and the bowels should be kept regularly open by the aid of mild

aperients. Counterirritation to the chest in the form of sinapisms or stupes is very beneficial. In the first stage, when there is little secretion, sedative expectorants—*ipsecac*, potassium citrate, and tartar emetic—are indicated. It is often necessary to add a sedative, such as opium or one of its derivatives (codein, $\frac{1}{8}$ – $\frac{1}{6}$ gr.—0.008–0.01 gm.) to allay the distressing cough. A combination such as the following will be found useful:

℞. Potassii citratis..... ʒiii (12.0 gm.)
 Vini ipsecacuanhæ..... fʒiiss (10.0 mils)
 Tincturæ opii camphoratæ..... fʒiii (11.0 mils)
 Succii limonis..... fʒss (15.0 mils)
 Syrupi..... q. s. ad fʒvi (175.0 mils).—M.
 Sig.—A tablespoonful every three or four hours.

When the secretion is more abundant, but still tenacious, ammonium chlorid is usually effective. It may be prescribed with brown mixture or syrup of squill. Balsamic expectorants—terpin hydrate, terebene, oil of eucalyptus, oil of santal and tar—are frequently of service in persistent attacks. Guaiacol carbonate (5 grains—0.3 gm. every three hours) is a valuable remedy when the exudation is purulent and abundant. Such combinations as the following often prove efficacious:

℞. Ammonii. chloridi..... ʒiss (6.0 gm.)
 Terpini hydratis..... ʒiss (6.0 gm.)
 Codeinæ sulphatis..... gr. iii (0.2 gm.).—M.
 Pone in capsulas No. xxx.
 Sig.—One or two every three hours.

℞. Terebeni..... fʒiiss (6.0 mils)
 Guaiacolis carbonatis..... ʒiss (6.0 gm.)
 Codeinæ sulphatis..... gr. iiss (0.16 gm.).—M.
 Pone in capsulas No. xxiv.
 Sig.—One every two or three hours.

Inhalations of medicated steam are useful when the cough is excessive. For young children the “croup kettle” is most convenient, but for adults the simplest plan consists in breathing deeply the warm vapor arising from the surface of boiling water. For the purpose a small amount of compound tincture of benzoin, eucalyptol or creosote may be dropped into a wide-mouthed jar half full of boiling water, and the vapor conducted to the mouth through a cone made of stiff paper or a folded towel.

In the aged and infirm alcoholic stimulants are sometimes required. Such tonics as cod-liver oil, iodid of iron, quinin and arsenic are useful during convalescence from severe and prolonged attacks. Much benefit is also obtained from a suitable change of climate.

CHRONIC BRONCHITIS

To meet with any measure of success, treatment must be directed largely toward the prevention of recurrent attacks, and the removal, if possible, of the underlying cause. Indiscriminate routine treatment is to be rigidly avoided. Change of climate, especially in winter, is most beneficial, and should be urged if the circumstances of the patient will permit. If there is much bronchial secretion a dry, warm climate, such as that of New Mexico or Southern California, in this country, and that of Egypt or the Riviera abroad, is generally to be recommended, whereas if there be little expectoration, a moist, warm climate, such as that of Florida, the West Indies, Madeira, Pau, or Algiers, is preferable. If patients are unable to avail themselves of the benefits to be derived from a suitable climate, they should remain indoors as much as possible in bad weather, and take every precaution against exposure. Flannel should at all times be worn next the skin, the feet should be kept perfectly dry, and the night-air should be avoided.

The diet should be simple but nutritious. In many cases alcohol in some form acts beneficially.

Underlying chronic diseases should always receive appropriate treatment. If cardiac insufficiency is present, digitalis alone or with strychnin may be required. If there is anemia with general malnutrition, such remedies as iron, arsenic, and cod-liver oil may be given with advantage. If gout is a factor, benefit may be expected from the administration of potassium iodid and alkalis. If renal inadequacy is coexistent, the diet must be very carefully supervised, and such measures adopted as will promote the functional activity of the various emunctories.

The *special remedies* most generally useful are the expectorants of a balsamic character, such as terpin hydrate, terebene, oil of eucalyptus, myrtol, and oil of santal. Tar is another remedy of value. It may be used in substance made into pills, or in the form of tar-water or the wine of tar. When the sputum is heavy and purulent, no drug usually acts so well as creosote or the carbonate of guaiacol. Potassium iodid is of service in some cases. It may be tried tentatively when the expectoration is very scanty and viscid, or when there is evidence of a gouty diathesis. If cough is excessive mild anodynes, such as codein or heroin, may be used from time to time to keep it in subjection. Alkalis (sodium bicarbonate, aromatic spirit of ammonia), with or without a few minims of the spirit of chloroform, taken in hot water before rising, will often lessen morning cough and facilitate expectoration.

Benefit is often derived from such combinations as the following:

℞. Terebeni
 Olei eucalypti
 Olei santali..... āā f ʒi-f ʒiss (4.0-6.0 mils)
 Codeinæ sulphatis..... gr. ii-iv (0.13-0.25 gm.)

Misce et pone in capsulas No. xxiv.

Sig.—One after each meal and at bedtime.

℞. Terpini hydratis..... ʒi (4.0 gm.)
 Guaiacol carbonatis..... ʒii (8.0 gm.)
 Strychninæ sulphatis..... gr. ss (0.03 gm.)
 Codeinæ sulphatis..... gr. ii (0.13 gm.)

Misce et pone in capsulas No. xxiv.

Sig.—One or two capsules three or four times a day.

Syrup of squill often acts remarkably well in acute exacerbations, especially if the concomitant emphysema is pronounced and the right ventricle is embarrassed. It combines the properties of an expectorant with those of a cardiac stimulant. Ammonium chlorid is an excellent adjuvant.

Inhalations are sometimes very efficacious, the most suitable remedies for this method of treatment being terebene, eucalyptol, oil of Scotch fir, creosote, compound tincture of benzoin, and spirit of chloroform.

℞. Chloroformi..... f ʒss-f ʒj (2.0-4.0 mils)
 Creosoti
 Terebeni
 Olei pini sylvestris..... āā f ʒiss (6.0 mils)
 Alcoholis..... q. s. ad f ʒj (30.0 mils)

Sig.—From 5 to 20 drops to be used in the inhaler several times a day.

Inhalations of compressed air may prove useful, especially in emphysematous subjects. *Intratracheal injections* have been employed with good results in some cases. From $\frac{1}{2}$ to 1 dram (2-4 mils) of a 1 per cent. solution of guaiacol or of a 2 per cent. solution of menthol in olive oil may be injected between the vocal cords into the trachea once a day, a syringe with a long curved nozzle being used for the purpose.

Occasionally, good results are obtained from the use of auto-genous *vaccines* in conjunction with other appropriate measures.

ASTHMA

The cause must be sought for and removed if possible. Patients who are sensitized to particular food proteins often remain free from attacks so long as the offending foods are kept out of the diet. Desensitization by subcutaneous injections of the

particular proteins is not often successful. Asthmatics who are sensitive to the proteins of horse dandruff and cat hair are not rarely relieved for months at a time by subcutaneous injections of these proteins, and asthmatics who are sensitive to the proteins of staphylococci may be benefited or even cured by vaccine treatment.

Vaccines of the predominant organisms occurring in the sputum are sometimes effective also in asthma resulting from bronchitis. The radical removal of foci of infection, wherever located, is indicated and may afford relief, especially in conjunction with treatment by autogenous vaccines. Removal of obstructions in the nose is sometimes curative, although in the large majority of cases the asthma returns in the course of time. In the case of horse asthmatics, it must be borne in mind that the subcutaneous injection of horse-serum, such as diphtheria antitoxin, may result in a violent or even fatal reaction, unless the patient is first desensitized by frequently repeated and gradually increasing doses. Although it is often impossible to meet fully the causal indication, much can be done to lessen the frequency and severity of the paroxysms. The diet should consist of plain, readily digestible food. The evening meal especially should be light. Vicissitudes of temperature must be carefully guarded against and flannel always worn next to the skin. In poorly nourished subjects tonics do much good. Change of residence sometimes proves of service, but the choice of locality must be determined largely by the personal experiences of the patient. Many sufferers do better in the smoky air of cities than in the country. Asthmatics with moist catarrh usually do well in a dry, warm climate, while those with dry catarrh generally derive more benefit from an atmosphere that is somewhat humid. Among empiric remedies potassium iodid holds the first place especially when the asthma is accompanied by chronic bronchial catarrh. To be effective, the drug must be given in doses of from 5 to 20 grains (0.3–1.3 gm.) three times a day for long periods. Tincture of belladonna (3–5 minims—0.2–0.3 mil—thrice daily) is sometimes a useful adjuvant to the iodid. Arsenic is well worth trying when the iodids fail. *Grindelia robusta* may be of service if there is much catarrh. Strychnin is of value in cases associated with emphysema. Occasionally the prolonged administration of bromids, by allaying the nervous erethism, seems to increase the interval between the attacks. Osborne speaks favorably of thyroid extract in asthma occurring in elderly persons with high bloodpressure.

The Attack.—The most suitable remedy for a particular case can only be determined by trial. Some patients derive great

benefit from the fumes of ignited stramonium or belladonna leaves or paper which has been impregnated with potassium nitrate. These agents may be burnt in the patient's room or smoked in a pipe or in the form of cigars. Occasionally, tobacco proves efficacious. Marked alleviation of the paroxysm is sometimes obtained from the inhalation of ethyl iodid (10–20 min.—0.6–1.3 mils). In some cases the attacks yield to a few whiffs of chloroform, although as a rule the effect of the drug is only temporary. The most reliable remedy in the large majority of cases is epinephrin (adrenalin) hydrochlorid in doses of 5 to 15 minims (0.3–1.0 mil) subcutaneously. The good effect may last as first two or three hours, but tolerance to the drug is gradually established and eventually it may fail to afford relief. In other cases benefit may be derived from the administration of belladonna, bromids, lobelia or quebracho by the mouth. Strong hot coffee is occasionally efficacious. If the attacks are accompanied by bronchial catarrh a combination such as the following may be of service:

R.	Sodii bromidi.....	℥iiss (10.0 gm.)
	Tincturæ belladonnæ.....	f ℥iiss (6.0 mils)
	Tincturæ lobeliæ.....	f ℥iii (11.0 mils)
	Fluidextracti grindeliæ.....	f ℥ss (15.0 mils)
	Aquæ menthæ piperitæ.....	q. s. ad f ℥iv (120.0 mils)

Sig.—A dessertspoonful in water every three hours.

Few attacks of asthma will resist the action of morphin or heroin hypodermically, but the greatest caution must be exercised in using these drugs lest a habit be established. Atropin is often of service and may be given alone or with morphin. The application of sinapisms or of dry cups to the chest sometimes has a good effect.

HAY-FEVER

The cutting of the weeds in the vicinity of the patient's residence often affords much relief. In New Orleans the vernal type of hay-fever is said to have been decreased more than 50 per cent. in one season by the enforcement of weed-cutting ordinances. Nasal abnormalities which favor a concentration of pollen in the nostrils should be corrected. Operation, however, should not be performed during the pollen season. Desensitization by means of specific pollen solutions yields good results in a fairly large percentage of cases. The best method is to begin the treatment at least three months ahead of the season of pollination and not to continue it through the season unless the prophylaxis fails. Only the pollen to which the patient reacts

by conjunctival or cutaneous test should be used for a vaccine. The injections should be given at intervals of not less than 3 or 4 days, the dose being gradually increased from the strongest dilution which fails to produce a positive cutaneous test to the strongest dilution (1 : 100) which gives a positive test. Maver, of the hay-fever clinic at Bellevue Medical College, reports good results from weekly injections throughout the year. If the treatment is carried out during the season considerable caution must be exercised owing to the danger of precipitating an anaphylactic attack. The highest dilution should be given at first and the succeeding doses very slowly increased. Not infrequently immunity is maintained only by giving an injection every 3 or 4 weeks during the season.

In the majority of cases removal to a region in which the disease does not prevail offers a sure means of avoiding the attacks or of obtaining complete relief if the symptoms have already appeared. Among the localities most frequently resorted to by residents of the Eastern and Middle states may be mentioned the White Mountains, the Adirondacks, and the lake districts of Maine and Canada. Many Americans escape their attacks by travelling in Europe. Owing to individual peculiarities a region that is well suited for one patient often brings no relief to another. A sea voyage affords complete immunity.

For patients who are unable to leave home a strict regimen, a daily tepid bath with friction of the skin, and the avoidance of dust, smoke and direct sunlight tend to make the hay-fever season more tolerable. Tonics, especially quinin, arsenic, and strychnin, are frequently useful. Atropin in doses of $\frac{1}{200}$ of a grain (0.0003 gm.) lessens the nasal secretion and relieves to some extent the dyspnea. A warm alkaline spray or an oil spray is often efficacious. A spray of epinephrin (adrenalin) solution (1 : 10,000) usually affords temporary relief, but when the effect of the drug wears off the discomfort is likely to be greater than it was before the treatment was used. Cocain should be avoided because of the great danger of establishing a habit. Boric acid washes usually relieve temporarily the itching of the eyes.

BRONCHOPNEUMONIA

(Catarrhal Pneumonia)

The open cold-air treatment, referred to under "Lobar Pneumonia," is less generally applicable to cases of bronchopneumonia, although in some instances, especially of the primary form and of that running a protracted course, it is very effective. In all cases the sick-room should be well supplied with fresh air without

drafts. In the case of very young infants a moist atmosphere is sometimes of great benefit and this may be secured by generating steam in an ordinary croup kettle. But whether the air is made moist or not it should be kept pure and, if possible, at a temperature not exceeding 70° F. Heavy, cumbersome bed-wraps should be avoided.

The diet should consist of liquid or semiliquid food. For children of more than three years and adults milk, junket, broths, soft-boiled eggs, and gruels are usually suitable forms of nourishment. For bottle-fed infants the milk strength should be reduced, as a rule, about one-third. Water must be freely given. In the more severe cases alcohol, in the form of whisky or brandy, well diluted, often seems to be of service. From 15 to 20 minims (1.0–1.3 mls), every three hours, for a child of 3 years, is usually sufficient.

In the absence of any special indication for local treatment, it will only be necessary to provide ample protection for the chest, and this may be done satisfactorily by means of a light jacket of cotton-wool. When the bronchitic feature is pronounced and there is much cough, mild counterirritation over the thorax is very useful. The desired effect may be produced by the application of mustard-plasters, care being taken to prevent them causing more than slight redness of the skin. Oil of turpentine, diluted with two parts of olive oil, and rubbed into the skin, is also a satisfactory means of producing rubefaction. Poultices of linseed meal or of clay through their weight make the breathing more difficult and are therefore harmful.

Hydrotherapy does good in many cases, especially in young children. As a rule, the tepid, warm, or hot tub-bath, at intervals of from 3 to 6 hours is the best form. Cold bathing, or even cold sponging, is not usually well borne. If the patient's temperature is high and his extremities are cold, which is often the case at the onset of severe attacks, or if at any time his circulation becomes especially feeble, he may be plunged for a minute or two into a hot bath (105° F.—40.5° C.). In other cases brief tepid baths (80°–90° F.—26.5°–32.0° C.) or warm baths (95°–100° F.—35.0°–38.0° C.) frequently serve to lower temperature, allay restlessness and promote sleep.

Drugs, judiciously selected with reference to the peculiar features of each case, are of great value. If the bronchitic element is prominent and the chest is full of râles expectorants may be given with advantage. The most generally useful expectorants are potassium citrate and ammonium chlorid. From 3 to 5 grains (0.2–0.3 gm.) of the former or from 1 to 2 grains (0.065–0.13 gm.) of the latter may be given every 2 or 3 hours to

a child of three years. If the bronchial secretion is very abundant, tincture of belladonna 1 minim (0.06 mil) every two hours is sometimes efficacious. If the child is unable to expel the accumulated mucus and the breathing in consequence becomes much embarrassed, an emetic dose of ipecac may afford relief. In debilitated children, however, the emetic should not be used. If the cough is very severe and persistent from 10 to 15 minims (0.6–1.0 mil) of paregoric may be given every two or three hours for a short period. Digitalis is indispensable when there are indications of circulatory failure. Two to three minims (0.1–0.2 mil) of the tincture every four hours is an average dose for a child of two years. For acute heart failure reliance must be placed upon subcutaneous injections of digipuratum or digalen, 1 to 2 minims (0.06–0.12 mil), camphor, $\frac{1}{4}$ to $\frac{1}{2}$ gr. (0.015–0.03 gm.) in sterile olive oil, or epinephrin, 3 to 5 minims (0.18–0.3 mil). Tympanites is to be treated by the applications of weak sinapisms to the abdomen, by anemas of asafetida, by enteroclysis with warm saline solution, by the use of a rectal tube, or by subcutaneous injections of phystostigmin— $\frac{1}{500}$ grain (0.00013 gm.)—or of liquor hypophysis—1 to 3 minims (0.06–0.18 mil)—for a child of three years. Inhalations of oxygen sometimes lessen cyanosis and make the breathing easier. Strychnin, $\frac{1}{200}$ grain (0.0003 gm.) every three or four hours for a child of two years, is also of benefit in combating respiratory failure.

During convalescence tonics and a change of air are often required.

PULMONARY EMPHYSEMA

The treatment of emphysema is chiefly that of the accompanying disease. The various means suggested for relief of chronic bronchitis may nearly always be used with advantage. If asthma is the primary disease, treatment directed toward lessening the frequency and severity of the paroxysms should be instituted. Violent exercises and overexertion of all kinds must be proscribed. A diet that is light and sustaining is indicated. All food likely to induce flatulence should be avoided. Much benefit is often derived from a change of climate, the choice of locality, however, depending somewhat upon the character of the complicating bronchitis. As a rule, high elevations are to be avoided.

The inspiration of compressed air with expiration into rarefied air by means of the pneumatic cabinet has been employed with variable degrees of success. Strümpell speaks favorably of

rhythmic compression of the lower portion of the thorax during expiration, as recommended by Gerhardt. This should be done systematically by another person two or three times a day during fifty or sixty respirations.

Tonics, such as iron and cod-liver oil, are required in some cases to improve the general health. Strychnin, being both a general tonic and a respiratory stimulant, is particularly useful. Digitalis is often of service when signs of cardiac insufficiency appear. Ammonium carbonate, in conjunction with strychnin and digitalis, usually has an excellent effect upon acute exacerbations of the bronchial catarrh. At such times sinapisms applied to the chest may also afford considerable relief. If sleep is disturbed by troublesome cough and oppressive dyspnea it may be necessary to give codein, heroin or even morphin. When the breathing is very difficult, the face suffused and livid, and the pulmonary circulation much impeded, recourse should be had to blood-letting, either local or general, according to the urgency of the symptoms.

EDEMA OF THE LUNGS

The treatment of *chronic pulmonary edema* coincides with that of the underlying disease. Cardiac stimulants are nearly always indicated. If the symptoms are severe aromatic spirit of ammonia may be given by the mouth and camphor subcutaneously. Dry or wet cupping of the chest is often very useful. Except in feeble subjects active purges may also be used.

The treatment of *acute pulmonary edema* must be prompt and energetic. A subcutaneous injection of atropin ($\frac{1}{100}$ – $\frac{1}{80}$ gr.—0.00065–0.0008 gm.) and morphin ($\frac{1}{6}$ gr.—0.01 gm.) is often very effective. It should be given at once and repeated in half an hour, if necessary. At the same time aromatic spirit of ammonia or brandy should be given by the mouth. Nitroglycerin may be of service if the arterial tension is high. Oxygen may afford some relief. Counterirritation by dry or wet cups or sinapisms is very useful, but when there is marked cyanosis venesection is preferable. The after treatment consists of rest, careful regulation of the diet, and, if there are symptoms of cardiac insufficiency, the use of such drugs as digitalis, caffein, strychnin, etc.

HEMOPTYSIS

Absolute rest is imperative. An ice-bag may be placed over the suspected site of the hemorrhage, but it is of doubtful value and should be removed if it aggravates the cough. Morphin, in

doses of $\frac{1}{12}$ to $\frac{1}{8}$ grain (0.005–0.008 gm.) hypodermically is of value in that it promotes tranquility and lessens irritative cough. Large doses, however, are objectionable, especially in tuberculosis, as they favor the retention of infected blood in the bronchi. Nitroglycerin is strongly recommended. It may do good by lowering the pressure in the pulmonary vessels. Small repeated hemorrhages seem to have been controlled in some instances by the use of saline purges. Among other remedies for which success has been claimed in long-continued bleeding, oil of erigeron, oil of turpentine and fluidextract of hamamelis may be mentioned. Ergot and tannin are useless and so is the inhalation of vaporized solutions of astringent drugs. Unless collapse is imminent stimulants of all kinds should be avoided. In cases of profuse hemorrhage bandages or elastic bands may be placed around the extremities, using sufficient pressure to impede the venous return without obstructing the arterial circulation. Artificial pneumothorax should be favorably considered in pulmonary tuberculosis if hemorrhages persist despite the usual methods of treatment and the site of the bleeding can be definitely determined.

PLEURISY

Patient should be kept in bed and restricted to a liquid or semi-solid diet. Free catharsis should be maintained throughout the attack. Pain is often relieved by the application of hot fomentations, sinapisms or turpentine stupes. Strapping the affected side from mid-spine to mid-sternum with broad strips of adhesive plaster, as originally suggested by Frederick T. Roberts, is also useful. Morphin is sometimes necessary. For excessive pain, however, no measure is so uniformly efficient as the application of a few wet cups.

Acute cases of pleurisy in robust subjects are often favorably influenced by the administration of salicylates, a method of treatment, which has been especially advocated by Aufrecht, Fiedler, Dock, and others. From 1 to $1\frac{1}{2}$ drams (4.0–6.0 gm.) of sodium salicylate should be given in the twenty-four hours, the dose being gradually reduced as the good effects become manifest. In asthenic, protracted cases of pleurisy the salicylates are of no avail and may prove harmful.

After the acute symptoms have subsided, the indications are to accomplish the removal of the fluid, to maintain nutrition, and to secure complete expansion of the lung.

Removal of Serous Effusion.—Counterirritation by means of iodine or small ("flying") blisters sometimes appears to promote

absorption. In vigorous subjects the administration of saline purgatives according to the method suggested by Matthew Hay may be tried, although it usually proves disappointing. The quantity of fluid consumed by the patient is restricted to a minimum, and every morning or every other morning from $\frac{1}{2}$ to 1 ounce (15.0–30.0 gm.) of magnesium sulphate is given in concentrated solution an hour before breakfast. Diuretics (theobromin, caffein, potassium citrate) and potassium iodid have been recommended, but they are of questionable value, and the latter may prove harmful by disturbing digestion.

Autoserotherapy has some champions, but the author's experience with it has not been very satisfactory. The method consists in reinjecting under the skin from 2 to 5 mls of the fluid aspirated from the pleural cavity. A sharp febrile reaction, accompanied by chill, often follows the injection.

While in many cases spontaneous absorption of the effusion eventually occurs, much saving of time is effected by early recourse to paracentesis. As a rule, this operation should not be delayed longer than 10 days or 2 weeks if the effusion is considerable and shows no signs of receding. The presence of fever is not a contraindication; indeed, the temperature frequently falls upon the removal of the fluid. Irrespective of the period of the disease paracentesis is demanded: (1) When there is sufficient fluid to induce marked dyspnea, cyanosis, persistent cough or other pressure symptoms; (2) when the fluid reaches the third rib and there is much displacement of the adjacent organs. The suspected presence of pus is also, of course, always to be regarded as sufficient ground for operative intervention.

Paracentesis Thoracis.—The patient should be brought to the edge of the bed, placed in a semirecumbent position with the thorax inclined slightly toward the healthy side, and supported by an assistant. The most favorable site for the puncture is usually the fifth or sixth intercostal space in the mid-axillary line or the seventh intercostal space near the post-axillary line. Care should be taken that the needle is aseptic, that the patient's skin at the site of puncture and the hands of the operator are surgically clean, and that the apparatus is in perfect working order. Local anesthesia, may be secured by means of a spray of ethyl chlorid. The needle should be inserted with a quick thrust along the upper margin of the rib, the depth of the puncture being gauged by the forefinger. As soon as a loss of resistance indicates that the point of the needle has entered the effusion, the valves opening into the aspirating jar should be opened and the stylet within the needle withdrawn. The needle having been introduced, the operator should satisfy himself that it is

freely movable, should hold it in position throughout the operation, and as the evacuation proceeds should slowly raise the exposed end so as to keep the inner opening below the level of the fluid in the pleural sac. The aspiration should be effected slowly, and at intervals it should be stopped by compressing the conducting tube. Too rapid evacuation may excite engorgement of the lung and edema.

The amount of fluid which should be removed depends somewhat upon the size of the effusion and the ease with which it can be evacuated. Even with large effusions it is rarely advisable to withdraw more than a quart (1.0 L.). The removal of small quantities is in many cases followed by the rapid absorption of the remainder. Under no circumstances should extreme efforts be made to obtain the largest possible amount of fluid. The operation should be terminated at once if incessant cough, severe pain, dyspnea, palpitation, tendency to syncope, or other untoward symptoms appear.

When the requisite amount of fluid has been evacuated, the needle should be withdrawn quickly from the chest, and the puncture closed with gauze and collodion.

If the exudate reaccumulate, aspiration may be repeated after the lapse of a week or 10 days. Free incision of the thoracic wall with thorough drainage has given good results in some cases in which the fluid has reaccumulated after repeated tapplings.

Occasionally, attempts at aspiration are unsuccessful. The cause of failure may be plugging of the canula, great thickening of the pleura, or encapsulation of the effusion. Under these circumstances it may be necessary to make repeated trials before a flow can be established. The aspiration of pleural exudates is rarely attended by accidents of any kind. Sudden death, the result of cerebral anemia, has been reported. Such an accident is not likely to occur if the evacuation be effected slowly and arrested immediately on the first appearance of any untoward symptom. Another grave and even fatal complication of thoracentesis, but also very rare, is a peculiar form of pulmonary edema, which is manifested by cough, intense dyspnea, and profuse albuminous expectoration. According to Riesman, who has collected 32 cases from the literature, the principal cause of this condition seems to be either too rapid or too great a withdrawal of fluid.

To Maintain Nutrition and Secure Normal Expansion of the Lung.—Throughout the course of the disease the patient's strength should be conserved by rest, fresh air, and good food. During convalescence tonics, such as iron, strychnin, cod-liver oil, etc., may often be prescribed with advantage. Systematic

respiratory exercises are of great value in favoring normal pulmonary expansion. The hygienic measures called for in early cases of pulmonary tuberculosis are also necessary after recovery from an attack of ordinary serofibrinous or fibrinous pleurisy.

Empyema.—The treatment of empyema is surgical. The indications are to evacuate the pus and to secure free drainage. If the effusion is merely cloudy and not distinctly purulent, thoracentesis may be tried and repeated once, with the understanding that surgical intervention will be required if the fluid continues to reaccumulate.

PNEUMOTHORAX

Unless the symptoms are pronounced no active treatment is indicated. At the onset morphin may be required to relieve pain, cough and dyspnea, and diffusible stimulants to combat the condition of collapse. Severe pressure-symptoms, however, demand intervention. Enough air should be removed from the pleural cavity by thoracentesis to relieve the tension, but forcible aspiration should be avoided, as a certain degree of pressure favors closure of the pulmonary fistula. In cases of valvular pneumothorax a free opening in the chest-wall may be necessary to secure relief. In hydropneumothorax the serous effusion should not be disturbed, at least for several weeks, unless it is causing discomfort and even then only enough fluid should be removed to relieve the intrapleural tension. In tuberculous cases the replacement of the fluid by nitrogen gas has sometimes proved very satisfactory. Pneumopyothorax is, as a rule, best treated by free incision and drainage, unless the condition of the patient's lungs is too far advanced to admit of such a radical procedure.

DISEASES OF THE CIRCULATORY SYSTEM

ACUTE MYOCARDIAL DISEASE

The indications are to arrest the inflammatory or degenerative process in the heart and to secure complete resolution, or if this is impossible, to favor the establishment of the highest degree of compensation attainable. The treatment consists largely of the measures that are called for by the causal condition and of absolute rest in bed. The patient should be kept at rest for several weeks after all symptoms of the primary infection have disappeared or until the rate and rhythm of the pulse are normal. Mental and emotional excitement must be avoided. Even after

the patient is permitted to be up and about his exertions should be restricted for a long period. The diet should be light and easily digestible, with the amount of fluids somewhat reduced. The bowels should be normally moved each day. In the early stages an ice-bag over the region of the heart often serves to allay palpitation and other local discomforts, but when there is much pain a sinapism or hot poultice may be more effective. Morphin is sometimes invaluable in controlling restlessness and procuring sleep. Digitalis may be of service, but in many cases it is useless or actually harmful. It must always be used tentatively. Attacks of acute heart failure are to be met with diffusible stimulants, such as aromatic spirit of ammonia, whisky or camphor. Caffein subcutaneously is sometimes helpful. Strychnin also may be useful. Adrenalin, in saline solution intravenously, has been recommended, but it should be used with great care lest through a sudden vasoconstricting effect it precipitate heart failure and pulmonary edema. During convalescence, tonics, especially iron, nux vomica and quinin, may be used with advantage.

CHRONIC MYOCARDIAL DISEASE

In the early stages of the disease treatment addressed to the causative condition not rarely serves to retard the progress of the myocardial deterioration. If there is definite evidence of syphilis antiluetic treatment is indicated; if a local focus of infection can be incriminated it should be removed, if possible; if hyperthyroidism is the causal factor thyroidectomy should be performed, unless the cardiac insufficiency is already too pronounced to justify the risk of operation; and if nephritis or hyperpiesis is the primary affection appropriate hygienic and dietetic measures are required. In many cases thorough investigation will reveal certain extrinsic factors which are contributing, more or less, to the cardiac embarrassment, such as tobacco poisoning, worry, insomnia, anemia, flatulent indigestion, etc. These, of course, should be removed if possible.

Rest and diet are important elements of the treatment. It is not always necessary that the patient should give up his occupation, but it is essential that the sum of his daily exertions should be adjusted to the working capacity of his heart. It must be borne in mind, too, that the fret and worry incident to many pursuits may exert as baneful an effect upon the circulation as undue physical efforts. In every case the rest of body and mind should at least be sufficient to allow the heart to recover the largest amount of reserve force of which it is capable. If the reserve

force of the organ is already spent, and, in consequence, breathlessness, palpitation, pain, etc., occur after slight exertion or even during repose, then absolute rest is imperative. On the other hand, young persons with organic mitral disease, especially mitral regurgitation, and others with fatty infiltration of the heart who give evidence of insufficient cardiac reserve force, but who present none of the symptoms of cardiac failure are often benefited by gentle exercise, such as walking on level ground, horseback riding, and playing at golf. In the early stages of degenerative myocardial disease, Swedish exercises and baths containing free carbonic acid gas, such as are used at Nauheim, are sometimes of service, but they must be employed tentatively, their effects upon the patient's pulse and subjective symptoms, being carefully observed. In elderly persons with atheroma of the vessels they are usually inadvisable and in cases of angina pectoris and of aortic regurgitation they are contraindicated. The Oertel treatment, which consists in walking a certain distance up a gentle incline each day, the distance and pace being gradually increased, is applicable only to cases in which the lesions in the heart are stationary and have not seriously compromised the integrity of the cardiac muscle.

A change of residence to a warm, dry, and equable climate, especially during the winter months, is often very efficacious when the deterioration of the heart muscle is not far advanced, but it is important that patients whose field of cardiac response is much reduced should be spared the trials of a long journey. The great benefit that frequently occurs from a sojourn at Nauheim, Carsbad, Bedford Springs or some other such resort is probably due more to the rest, good air, freedom from customary vexations, and strict diet and regimen than to any special form of hydrotherapeutic or gymnastic treatment. Whatever climate is selected high elevation should, as a rule, be avoided.

As with rest and exercise so with diet, no hard and fast rules can be laid down. The diet must be carefully adapted, however, to the digestive powers and needs of the system. Rich foods, bulky foods and foods that induce flatulence are clearly inadmissible. The dinner should be at midday and in all cases the supper should be extremely light. The question of the quantity of food is also one of great importance. In pronounced heart-failure the diet must, of course, be much restricted and the food given in small quantities at comparatively frequent intervals. Degenerative changes in the heart usually occur at a period of life when the amount of food may be considerably reduced without impairing the general nutrition. In certain cardiac cases with edema and chronic nephritis a salt-free diet is efficacious. Balfour, Allbutt

and others have dwelt upon the advisability of restricting the amount of liquids taken with meals in cases of cardiac insufficiency. By this means the tension in the venous system may be lowered and the arterial resistance reduced. Judgment, however, must be exercised in the matter of drink, as the amount of fluid required to secure a free evacuation of waste products from the system must vary in different cases.

Tea and coffee should be used sparingly, if at all. Alcohol is better dispensed with. The use of tobacco should be limited, and in pronounced myocardial insufficiency it should be avoided. Excesses of all kinds must be interdicted. The bowels should be normally moved each day. For the purpose, if necessary, a vegetable cathartic should be given at night or a saline in the morning. This may be supplemented from time to time with advantage by a pill of blue mass. Sometimes no single remedy affords such prompt relief from the general distress as a mercurial laxative. If the patient is anemic and his general nutrition poor such tonics as iron, arsenic and strychnin may often be given with advantage. Among special remedies for myocardial insufficiency, digitalis holds the first place and is indicated irrespective of what form of valvular disease may be coexistent. For administration by the mouth a good standardized tincture, a freshly prepared infusion, and powdered digitalis are, as a rule, the best preparations. Nativelle's digitalin and digipuratum are efficient proprietary preparations. One of Nativelle's granules ($\frac{1}{4}$ milligram) is equivalent to about 15 minims (1.0 mil) of the tincture. Digipuratum, which is an alcoholic extract of digitalis, free from digitonin and other inactive substances, is supplied in tablet and liquid forms. Each tablet represents $1\frac{1}{2}$ grains (0.1 gm.) of digitalis and 15 minims (1.0 mil) of the liquid is equivalent to $1\frac{1}{2}$ grains of digitalis. Liquid digipuratum is a reliable preparation for subcutaneous or intravenous injection.

The best results from the use of digitalis are in cases of auricular fibrillation with dyspnea and a frequent irregular pulse. Whether edema is present or not is immaterial. In decompensation with a frequent pulse but a normal rhythm digitalis is less reliable, although it often proves decidedly useful, especially if there is edema and the urine is scanty and concentrated. In both of these conditions the drug should be pushed until the desired effect is obtained or signs of intolerance appear. From 10 to 15 minims of the tincture three times a day will often be sufficient. If nausea, vomiting, diarrhea, headache, or "coupling of beats" occurs the drug should be discontinued and not resumed until the untoward symptom has disappeared. Otherwise it should be continued until the pulse falls to about 70, when it should be

stopped for several days and then, if the pulse again becomes frequent, resumed in smaller doses, the amount being changed from time to time in order to determine the exact dose that will control the heart without producing a toxic effect. In auricular fibrillation it is usually, but not invariably, necessary for the patient to continue taking the remedy more or less regularly for the remainder of his life.

Recent studies have shown that quinidin, an isomer of quinin, may actually abolish auricular fibrillation by depressing irritability and conduction in the auricular muscle. Digitalis does not affect fibrillation itself, but it tends to lower the rate of the ventricular contractions and to restore the normal rhythm by depressing the conductivity of the His bundle. Quinidin, however, being depressant to all the cardiac functions, is not so generally useful as digitalis. It is not all suitable for ambulatory patients and must be used with great care if decompensation is pronounced. Moreover, the drug frequently causes nausea and vomiting and in some instances its effects are distinctly unfavorable. It restores the normal rhythm in from 40 to 50 per cent. of the cases, although a relapse usually occurs in from a few days to several months. Three grains (0.2 gm.) of the sulphate may be given on the first day as a test for idiosyncrasy and then the dose may be gradually increased to 5 grains (0.3 gm.) or, if necessary, to 10 grains (0.6 gm.) three or four times a day. The treatment should be suspended whenever severe headache, precordial distress, palpitation, increased dyspnea, pronounced tinnitus or vertigo, or other untoward symptoms develop.

In cases of pronounced myocardial degeneration occurring in elderly persons (so-called senile heart) digitalis is not infrequently useless and may be actually harmful, although it is sometimes of service when given in small doses, that is, 5 minims (0.3 mil) of the tincture or $\frac{1}{2}$ grain (0.03 gm.) of the powdered drug, two or three times a day, or one granule ($\frac{1}{4}$ milligram) of Nativelle's digitalin at bedtime.

Neither partial nor complete heart-block in itself contraindicates the use of digitalis if there are also evidences of cardiac insufficiency, but it always dictates cautious administration. Although the drug has some tendency to excite extrasystoles, the occurrence of these premature beats is not a contraindication if other conditions are also present in which digitalis is likely to be of service. The height of the blood pressure is immaterial; indeed, in hyperpiesis when the heart is overborne by the excessive labor and gives evidence of yielding, the administration of the drug may prove a valuable addition to eliminative and dietetic measures and rest. Finally, neither aneurysm of the aorta nor

arteriosclerosis should be considered a bar to the use of digitalis, if its employment is dictated by changes in the heart itself.

When digitalis fails other cardiac tonics rarely succeed. Strophanthus may be tried, but it is less certain of absorption than digitalis and therefore less reliable. Strychnin has been shown to have no important effect upon the heart or bloodvessels in therapeutic doses; nevertheless it is often of value in chronic myocardial disease, especially in the myocardial insufficiency incident to old age. It is likely that the good effects of the drug are due to an improvement in the general muscular tonus brought about by its action on the central nervous system.

Acute Heart Failure.—Diffusible stimulants, such as alcohol, ammonia and camphor are of service. Alcohol may be given in the form of brandy or whisky, in doses of $\frac{1}{2}$ ounce (15.0 mls), undiluted and preferably hot; ammonia may be used as the aromatic spirit of ammonia in doses of 15 to 30 minims (1.0–2.0 mls), in half a tumbler of water; and camphor should always be given subcutaneously, 15 to 30 minims (1.0–2.0 mls) of a 10 per solution in sterile olive oil being injected at intervals of an hour. In urgent cases a remarkably good effect is sometimes produced by injecting strophanthin into a muscle or preferably into a vein, but under no circumstances should this drug be employed if the patient has been taking digitalis by the mouth within 5 or 6 days. The dose of the official preparation is $\frac{1}{80}$ grain (0.00075 gm.) in 2 drams (8.0 mls) of normal salt solution. It should not be repeated before 48 hours. Inhalations of oxygen sometimes make the patient more comfortable. Hot applications over the heart act beneficially.

When the right ventricle is greatly distended as indicated by severe dyspnea, cyanosis, and an increase in the area of cardiac dulness to the right, the abstraction of from 10 to 15 ounces (300–450 mls) of blood from the median basilic vein is very useful.

Edema.—In many cases absolute rest, the restriction of liquids to 1500 mls a day, the withholding of salt from the food as far as possible, and the administration of digitalis suffice to remove the edema. Purgatives are of value, but some caution must be exercised in their employment lest they prove exhausting to the patient. The salines and compound jalap powder are usually the best. Diuretics are also useful. The most effective in conjunction with digitalis are caffeine, theobromin, theocin and the organic salts of potassium. The following mixture of potassium acetate with the infusion of digitalis often acts well:

R. Potassii acetatis..... ʒiii (10.0 gm.)
Infusi digitalis..... f ʒiii (90.0 mls)

Sig.—A dessertspoonful three times a day.

Another time-honored remedy is Guy's or Niemeyer's pill, consisting of a grain (0.65 gm.) each of powdered digitalis, powdered squill and blue mass. One pill should be given three times a day, after meals, for several days, the condition of the mouth being carefully observed for evidences of salivation. In some cases caffen or theobromin may be added to the other ingredients with advantage, as in the following prescription:

℞. Pulveris scillæ
 Pulveris digitalis
 Massæ hydrargyri..... āā gr. xx (1.3 gm.)
 Theobrominæ..... ʒj (4.0 gm.)
 Ponē in capsulas No. xx.
 Sig.—One three times a day, after meals.

The application of smooth firm bandages to the swollen limbs sometimes affords much relief. In extreme cases the Karell diet is well worth trying. Briefly stated, it consists in giving 200 mils of milk at intervals of 4 hours from 8 o'clock in the morning until 8 o'clock in the evening. No other food or liquid is allowed. If there is much thirst the patient may be permitted to rinse out his mouth with water at intervals and if hunger is urgent a small piece of dried toast may be given with each portion of milk. If pleural effusion or ascites is pronounced, and especially if it is causing respiratory embarrassment, paracentesis should be practised. When all other measures have failed recourse may be had to scarification of the most swollen and dependent parts, to the insertion into the subcutaneous tissue on the posterior aspect of the leg on either side of the tendo Achilles of fine silver cannulæ (Southey's tubes) with rubber tubes attached, or to incisions about 2 inches in length behind the inner malleolus on each side. These methods often serve to draw off large amounts of fluid, and thus to relieve the tension in the venous circulation, although they may increase the patient's discomfort and unless carried out with great care as to asepsis are likely to be followed by erysipelatous inflammation.

Dyspnea.—Chief reliance must be placed upon those measures that have already been recommended as useful in restoring the balance of the circulation. Dyspnea excited by flatulent distention of the stomach is often relieved by carminatives—Hoffmann's anodyne, spirit of chloroform, spirit of mint, etc. Dry or wet cupping over the back of the chest or venesection may give great relief when there are signs of pulmonary engorgement. Aspiration will be required if there is considerable pleural effusion. When the arterial pressure is high nitroglycerin may prove efficacious. Oxygen is sometimes useful. In severe cases morphin hypo-

dermically ($\frac{1}{8}$ – $\frac{1}{4}$ gr.—0.008–0.016) is often the only resource. In paroxysms of acute pulmonary edema (cardiac asthma) occurring at night, a combination of morphin and atropin is invaluable.

Palpitation.—Rest is often required. Locally, an ice-bag, a sinapism, or a large belladonna plaster may afford relief. Occasionally small doses of aconite are of service. When flatulence is the exciting cause, carminatives will be found efficacious. Palpitation of nervous origin is usually benefited by bromids. If the attacks are very severe and interfere with sleep it may be necessary to use morphin.

Cardiac Pain.—Temporary precordial oppression is often relieved by a warm or cold application or a sinapism and the administration of hot whisky, aromatic spirit of ammonia or Hoffmann's anodyne. Dull continuous pain in the upper part of the chest may be favorably influenced by a nitrite or an iodide, even if the arterial pressure is not high. Persistent pain and tenderness over the epigastrium and right hypochondrium, the result of venous stasis in the stomach and liver, may yield to local cupping or leeching and the administration of a mercurial purge. The treatment of angina pectoris is discussed on p. 668.

Insomnia.—Restriction of the evening meal to small amounts of the simplest kind of food is helpful. Of the milder somnifacients bromids (10–20 gr.—0.6–1.3 gm.), barbital (5 gr.—0.3 gm.), and chloralamid (10–20 gr.—0.6–1.3 gm.) are the safest and best. A combination of barbital and codein sometimes acts very well. Bramwell has found paraldehyd useful in cases of myocardial insufficiency with bronchitis. When there is high arterial pressure nitroglycerin alone or in combination with a bromid is often efficacious. On the whole, no remedy is so generally useful as morphin, especially when sleeplessness is associated with pain, precordial distress, anxiety and restlessness. One-sixth of a grain (0.01 gm.) with $\frac{1}{150}$ grain (0.0004 gm.) of atropin is often sufficient.

Vomiting.—This may be due to faulty diet or to digitalis or other drugs. In many cases, however, it is the result of venous stasis in the stomach. In severe cases it is advisable to rest the stomach. No food should be given by the mouth except iced champagne, whey, albumen water, milk and lime-water or peptonized milk.

Calomel is often indicated. Dry or wet cupping is of benefit when the liver is enlarged and tender. Antiemetics are not often efficacious, but bismuth subcarbonate or cerium oxalate may be tried. About 10 grains (0.6 gm.) of either drug may be given half

an hour before feeding. In obstinate cases rectal feeding may become necessary.

ANGINA PECTORIS

The treatment of angina pectoris in the intervals between the paroxysms is for the most part that of the arterial or cardiac disease of which the angina is only a symptom. Secondary influences which may have been exhausting the heart itself or irritating the nerve centers should be sought for and removed. In all cases it is imperative that the patient should lead a quiet, easy life, should avoid as far as possible all mental and physical excitement, and should abstain from the use of tobacco and alcohol, and, as a rule, from that of coffee. The element of rest is of vital importance, but good judgment is required in determining how complete it shall be and for what period of time the inactivity, relative or absolute, shall be enforced. If the attacks are frequent and easily provoked, or if there is much breathlessness, the patient should be advised to keep in bed. On the other hand, if the seizures do not occur frequently or readily, and there is no indication of cardiac exhaustion, exercise need not be altogether foregone. Walking is the best form of exercise, but it should be on flat ground, and never against a strong wind. Gentle massage, and even a few passive movements, may sometimes be attempted even in bedridden patients, but resistance exercises as well as the Nauheim baths are inappropriate.

The question of diet is scarcely less important than that of exercise. Small meals of readily digested food are to be recommended. Meat, as a rule, should be used sparingly. Hot breads, fried meats, greasy pastry, coarse vegetables, and highly seasoned dishes are inadmissible. The evening meal especially should be light. Muscular exercise and mental excitement of any kind after meals are particularly injurious. The bowels should be kept regularly open, mild aperients being used for the purpose if necessary.

Between the attacks no drug is so generally useful as potassium iodid, although the manner of its action is not definitely known. It is most effective, of course, in cases of syphilitic origin, but it is not without a beneficial action in angina from other causes. However, in aged persons, in whom the cardiac pain is but one of the manifestations of the involutionary changes taking place in the arteries, the iodid is of little value. To be effectual in any case the drug must be given for a considerable period of time. Except in case of syphilis, doses of 10 grains (0.6 gm.) three times a day are usually sufficient. Next to the iodid no remedy is so

serviceable as nitroglycerin. It often does good even when the bloodpressure is not high. It acts favorably by relaxing the coronary arteries, although by depressing the vagus it tends also to improve the tonicity and contractility of the heart. Nitroglycerin and other vasodilators must be used with considerable caution, however, in cases of chronic nephritis with hypertension. In cases in which excessive nervous irritability is a conspicuous feature, bromids in full doses are indispensable. Digitalis has no place in the treatment of angina pectoris itself. It should be reserved for the menacing effects of cardiac dilatation. Alone or in association with theobromin, it is also of service in cases of hypertension when the urine becomes scanty and uremia seems imminent. In anemic and debilitated patients tonics, especially arsenic and iron, are very useful. Finally, any constitutional disease that may be present, such as gout or syphilis, must receive appropriate treatment. Arsphenamin was formerly believed to be contraindicated in cardiovascular syphilis, but it is now known that if the drug is given at first in small doses (0.2 gm.) and the amount cautiously increased, it is safe and often of value. Its use should always be followed by that of mercury and an iodid.

The Attacks.—When attacks are brought on by indigestion, they can frequently be staved off by the timely use of a brisk mercurial or saline laxative. Flatulency should be met by the administration of a stimulant carminative, such as whisky, aromatic spirit of ammonia, or spirit of ether. For the relief of the pain no remedy is so useful as amyl nitrite. In the majority of cases a mere whiff of this speedily arrests the paroxysm. The patient should carry the remedy on his person in a small vial or better in the form of glass "pearls," containing from 3 to 5 minims (0.2–0.3 mil) which can be broken in a handkerchief and the vapor inhaled, as soon as he perceives the pain. For mild attacks a drop of the spirit of nitroglycerin on the tongue is sometimes sufficient. If the paroxysms are severe and prolonged, morphin and atropin should be given hypodermically. If amyl nitrite and morphin fail, recourse may be had to the inhalation of chloroform, but the use of this drug is attended with a certain degree of risk. It is especially dangerous if the bloodpressure is low and symptoms of shock accompany the pain. The application of a mustard-plaster to the precordial region is sometimes useful in cases in which the attacks are prolonged or occur in rapid succession. Cardiac depression following a paroxysm should be combated by such drugs as camphor, strychnin, and caffein, and if necessary, by the inhalation of oxygen. After severe attacks it is necessary to enjoin rest in bed for several days.

ACUTE BENIGN ENDOCARDITIS

The treatment of acute endocarditis is mainly that of the causal condition and of acute myocarditis (see p. 660). Too much emphasis cannot be given to the need of frequent examination of the patient's heart during the course of all acute infections, in particular of acute articular rheumatism, even of the mildest type (see page 595). The special indication is to secure complete resolution of the inflammatory process or, if this be impossible, to favor the establishment of the highest attainable degree of compensation. *Prolonged and complete rest* is the most important factor of the treatment. The patient should be confined to bed not only during the attack, but for several weeks after it has subsided, in order to allow sufficient time for the damage to be repaired or for compensatory hypertrophy to be thoroughly established. In the period of convalescence extraordinary efforts are often required to prevent those indiscretions which are so liable to cause a fresh invasion of the valves or to strain the already overburdened heart. Mental and emotional excitement must also be avoided as much as possible, since they both tend to increase the force and frequency of the pulse. The diet should be liquid and unstimulating. For a week or two milk is the most appropriate food; later milk-toast, eggs, thin gruels, light broths, and steamed rice are admissible.

Externally, an ice-bag is often useful in allaying excitement of the heart. Internally, at the outset and from time to time throughout the illness, mild mercurial or saline aperients may be used for their depurative effect. Digitalis may be of service when the pulse is weak and irregular, but in the large majority of cases this remedy is not indicated. Heart failure is to be combated by such stimulants as alcohol, ammonia, strychnin, and caffeine. Morphin is sometimes required to relieve severe pain, allay nervous perturbation, and to promote sleep. To these measures is to be added, of course, the treatment appropriate to the disease upon which the endocarditis has supervened.

Treatment by continuous vesication and the prolonged administration of potassium iodid has seemed to most practitioners of large experience to be of doubtful utility, although it has been advocated by Pepper in this country, André Petit in France, Rosenstein in Germany, and Walsh and Caton in England.

Caton, especially, has presented some very strong evidence in favor of these measures as auxiliaries to prolonged rest in bed. He reports that of 39 cases of acute endocarditis treated by this method, 29 left the hospital with normal heart-sounds and 10 with a bruit, and that of 13 treated expectantly 12 left the hos-

pital with a bruit. Many of the cases were kept under observation subsequently for a long period, and every care was taken to make the observations accurate.

ACUTE MALIGNANT ENDOCARDITIS

The treatment is largely that of the initiating septic infection. In some cases of streptococcal origin an anti-serum seems to have been of service, but generally the results of this method of treatment have been unfavorable. Autogenous vaccines have not proved successful. The administration of quinin in moderated doses has frequently been recommended. Symptoms of cardiac failure should be treated on the lines laid down for acute myocarditis (see p. 660).

SUBACUTE INFECTIVE ENDOCARDITIS

(Chronic Infective Endocarditis)

Any primary focus of infection which may have been concerned in producing the endocarditis should be removed, if possible. Autogenous vaccines are not likely to prove of value, although some writers have reported favorably upon their use. Capps and Billings have recently reported good results from the use of sodium cacodylate subcutaneously in doses of 2 to 4 grains (0.13–0.26 gm.) a day over a long period. Of 8 cases cited by Capps, all of which showed positive blood cultures, 4 were well after intervals of from 22 months to 11 years, and 2 were improved after an interval of 3 and 6 months respectively. The general treatment is that of acute simple endocarditis (see p. 670).

CHRONIC VALVULAR DISEASE

(Chronic Endocarditis)

During the period of compensation the aim should be to promote in every way the nutrition of the heart muscle and to eliminate all conditions that may throw an undue strain upon the heart or that may increase the already existing valvular defect. The patient's whole manner of life must be carefully reviewed and his work, both mental and physical, his rest, his recreation, and his diet adjusted to the reserve power of his heart. Excesses of every kind should be avoided and emotional strain, anxiety and worry reduced to a minimum. The food should be nutritious and easily digestible. The importance of securing regular action of the bowels, of keeping the skin active by fre-

quent bathing and of protecting the body by suitable clothing should be emphasized. Exercise in the fresh air should be encouraged, but whatever its nature, the amount should always be less than that which gives rise to sensations of discomfort. Finally, any focal infection, because of its power to depress the heart and to excite recurring attacks of endocarditis, should be removed, if possible.

After the occurrence of decompensation, the treatment resolves itself into that of myocardial insufficiency, which is fully considered on p. 661 *et seq.*

ACUTE PERICARDITIS

Absolute rest of body and mind is essential. During the first week, at least, milk is the most suitable form of nourishment. Of local applications, none is so generally useful in allaying pain and palpitation as the ice-bag. If cold is not well borne hot fomentations may be substituted. In cases with very severe pain the application of a few wet cups or of a fly-blister frequently affords relief. Morphin is sometimes necessary. In addition to relieving pain, it lessens restlessness and promotes sleep. In rheumatic cases salicylates should be continued. The routine administration of cardiac stimulants is objectionable, but such drugs as digitalis, caffein, and camphor are necessary when signs of cardiac weakness develop.

Stage of Effusion.—In the serofibrinous cases if the exudate is slight and causes no discomfort, an expectant plan of treatment may be safely employed. If the effusion is considerable, but is without serious effects upon the heart treatment by counterirritation, a dry diet, and the administration of purgatives and diuretics may be tried, although it frequently fails of its purpose.

If the effusion proves menacing or persists after a thorough trial of medicinal treatment, paracentesis pericardii should be performed. As to the best site of the puncture, there is no uniformity of opinion. The point most commonly recommended is the fifth left intercostal space, to the outside of the internal mammary artery, or about one inch from the border of the sternum. A point equally good, if not better, especially if the heart sounds and friction are well heard, is in the fifth intercostal space just inside the lateral border of cardiac dulness. A puncture at this point is not likely to enter the pleura, as the lung is usually pushed well to the left by the effusion. Another point recommended by some writers is the left costo-xiphoid angle, the needle being thrust upward and backward close to the costal margin. A

preliminary incision through the skin under local anesthesia is advisable if pyopericardium is suspected. Puncture of the right ventricle has not been infrequent in attempts at paracentesis. Fortunately, however, this accident has rarely caused serious consequences, although Broadbent cites two instances in which it resulted fatally through hemorrhage. It is unnecessary, and often inadvisable, to withdraw all of the effusion. The removal of a portion lessens the pressure within sac and thus permits the remainder to be absorbed.

In pyopericardium free incision with drainage is indicated, and paracentesis should be restricted to diagnostic purposes. The mortality of cases treated surgically is at least 50 per cent.

The period of convalescence requires careful attention. The absolute rest should be continued until all evidences of the disease have disappeared, and for many months afterwards no effort should be permitted that is likely to cause the least cardiac strain.

ARTERIOSCLEROSIS

The chief indications are to remove, if possible, the causes which have led to the disease and to keep the bloodpressure within bounds. The regulation of the diet is very important. Stimulating foods must be interdicted. Generally speaking, a diet that is relatively rich in vegetables and cereals is best suited. Even more important than the quality of food, however, is the quantity. As Mitchell Bruce has said, the chief maxim of the dietary is not to avoid this or to eat that but to observe strict moderation in all things. Alcoholic beverages should be prohibited and tobacco used sparingly, if at all. As far as is possible the patient should be protected from all unnecessary excitement. A course of treatment at one of the well-known spas or even a change of scene often exercises a beneficial influence upon the disease, and doubtless largely by securing mental tranquility. All physical over-exertion must be rigidly avoided, although moderate systematic exercise in the open air should be encouraged, unless the blood pressure is excessively high or there are manifestations of cardiac insufficiency. When active exercise is contraindicated gentle massage may prove of service.

Drugs, as a rule, play only a secondary part in the treatment. In syphilitic arterial disease, especially aortitis, arsphenamin should be given cautiously and in small doses, and followed by mercury and iodids. Even in the absence of syphilis, iodids, if given in moderate doses and for a considerable period, sometimes seem to do good in the premature forms of the disease. Perhaps no single measure, is so uniformly beneficial, however, as

the periodic use of a pill of blue mass at bedtime, followed by a saline cathartic in the morning.

High bloodpressure is best controlled, as a rule, by dietetic and hygienic measures, nitroglycerin and other powerful vasodilators being reserved for such emergencies as dyspneal or anginal attacks. Excessive arterial hypertension may require absolute rest, a spare diet, preferably of milk, free catharsis and blood-letting. Bromids, if given in moderate doses and at bedtime, are often useful in allaying nervous irritability and promoting sleep. When symptoms of cardiac insufficiency appear the treatment becomes that of chronic myocarditis (see p. 661).

ANEURYSM OF THE AORTA

The treatment of aortic aneurysm is, on the whole, unsatisfactory. The indications are to arrest the destructive luetic process in the arterial wall, to promote clotting within the sac, and to relieve distress. If the case is a recent one and there are no evidences of cardiac insufficiency, courses of arsphenamin and mercury should be employed with the hope of destroying the spirochetes in the vascular tissue. In any case an attempt should be made to reduce the blood pressure within the aneurysm and thus favor the formation of a clot. For this purpose the treatment suggested by Tufnell* may be followed more or less closely, although actual cure cannot be expected from it. The chief elements of the treatment are *rest* and *restriction of diet*. The patient should be kept in bed for a period of from 6 weeks to 3 months, being allowed to get up only to use a commode. Mental excitement of any kind must be avoided. The diet as outlined by Tufnell consists of 2 ounces (60 gm.) of bread and butter, with 2 ounces (60 mls) of milk or tea for breakfast and supper, and 2 or 3 ounces (60–90 gm.) each of bread and meat, with from 2 to 4 ounces (60–120 mls) of milk or claret, for dinner, but it has been found that these amounts of food are inadequate and that a more liberal allowance of solids may be made without detracting in any way from the efficiency of the treatment.

During the period of rest aperients are usually necessary to obviate constipation and the injurious effects of straining in defecation. The employment of gelatin subcutaneously to promote coagulation, as recommended by Lancereaux, was found to be of little value and has virtually been discarded. Potassium iodid, first suggested by Bouillaud, unquestionably relieves pain in many cases, but the manner of its action is not known. It should be given in doses of 10 to 20 grains (0.6–1.3 gm.) thrice

* Tufnell, Treatment of Internal Aneurysm, 1864.

daily. The withdrawal of from 15 to 20 ounces (450–600 mils) of blood may be of service when there is severe pain or dyspnea. Cold applications are also helpful, but in many cases recourse must eventually be had to morphin.

The method of treating aortic aneurysms by means of fine wire introduced through a hollow needle into the sac was first suggested by C. H. Moore,* in 1864. Corradi,† in 1879, demonstrated that the procedure could be made more effective by passing a galvanic current through the wire, thus producing more rapid and firm coagulation. The operation entails comparatively little risk when performed by an experienced operator and often yields very satisfactory results, almost always relieving pain and in some cases apparently prolonging life. It is only suitable, however, for sacculated aneurysms. The technique of the procedure is described on p. 525.

ARTERIAL HYPERTENSION

(Hyperpiesia)

As arterial hypertension is the result of causes that are not definitely known and seems to be in itself a compensatory process, the chief problem of its management is the protection of the patient from all deleterious influences, especially physical, mental and emotional strain, dietetic excesses, and intercurrent infections. It is not always necessary or advisable for a man of important affairs to give up his business completely, but it is necessary to effect such readjustment in his everyday life that he may secure more opportunities for mental and physical relaxation. When there is a sudden accession of hypertension, when pronounced myocardial symptoms appear, or when there are premonitions of cerebral accidents, rest in bed for a week or ten days is usually imperative. On the other hand, in comparatively robust individuals, with no symptoms referable to the heart or brain, carefully graduated exercise in the fresh air is often decidedly useful. As to the amount of exercise the functional response of the myocardium must be the determining factor. High blood pressure is no indication of nitrogen retention, and, therefore, if the functional capacity of the kidneys is normal, it is unnecessary to cut out all proteins. It is necessary, however, to lessen materially the total intake of all food, and undoubtedly many patients are better off on diet that is relatively low in proteins. Obese subjects, especially do well upon a reducing diet. Alcoholic drinks are undoubtedly harmful and so is

* Trans. Med. Chir. Soc., Lond., 1864, xlvii.

† La Sperimentale, April, 1879.

tobacco in excess, but in many cases 1 or 2 mild cigars a day may do less harm than the discomfort that would result from their withdrawal.

Climate is not without influence. The majority of patients who have symptoms are more uncomfortable in winter than in summer, and therefore a change to a warm climate during the cold weather is desirable, although, of course, it is not always feasible. Turkish baths or other sweating procedures, if not used too frequently, may be of service in patients who are still robust and who show little that is abnormal besides the hypertension. It has not been proved that the condition of the bowels has anything to do with the blood pressure, nevertheless it seems desirable to promote elimination in every way and, therefore, if there is any tendency to constipation, it is advisable to prescribe mild cathartics and to give at intervals of ten days or two weeks a pill of blue mass and a saline.

There is no medicinal treatment for hypertension itself. Potassium iodid is usually recommended, but it is doubtful whether it has any decided influence upon the condition. In climacteric hypertension endocrine therapy, especially the administration of ovarian extract, is sometimes useful in conjunction with rest and bromid medication. Vasodilators, such as nitroglycerin, sodium nitrite, and erythrol tetranitrate are best reserved for emergencies, when the heart or the cerebral vessels give the signal. They are often invaluable when there is embarrassment of the heart, anginoid pain, or unwonted fulness in the head. In vigorous patients with inordinately high bloodpressure venesection, to the extent of 10 to 15 ounces of blood, sometimes produces very satisfactory results. The d'Arsonval high frequency current often acts favorably, but its effects are, as a rule, transitory. If insomnia calls for active treatment, barbital, a combination of potassium bromid with hydrated chloral, 10 or 15 grains (0.6–1.0 gm.) of the former with 5 grains (0.3 gm.) of the latter, will usually be found useful. Patients with definite myocardial insufficiency require absolute rest, careful regulation of diet, and liberal doses of digitalis. Not rarely theobromin will be found a useful adjuvant to digitalis.

ARTERIAL HYPOTENSION

The treatment of persistent hypotension varies with the cause. In all cases the patient's habits and method of living must be carefully reviewed. If ready physical exhaustion is the dominant feature, rest is important; on the other hand, if the tendency is to mental rather than physical tire, systematic exercise may

produce excellent results. In both groups of cases hydrotherapy is invaluable. If myocardial weakness is a factor digitalis is likely to prove efficacious. In the anemic iron and other tonics are useful. Organotherapy is not often of service, although ovarian or corpus luteum extract may sometimes be given with advantage in hypotension developing at the menopause and epinephrin or an extract of the suprarenal gland may occasionally be of benefit when hypotension is accompanied by features suggestive of Addison's disease. Timme describes a pluriglandular syndrome, characterized by intratemporal headache, great fatigability, low blood pressure, low blood-sugar content, abnormalities of skeletal growth and usually sex deficiencies, in which pituitary gland products cause marked improvement.

DISEASES OF THE KIDNEYS

ACUTE NEPHRITIS

It may be possible in some instances to prevent the occurrence of nephritis in acute infections by restricting the diet to bland foods, withholding irritant drugs of all kinds, protecting the body against chilling, promoting the functional activity of the skin and intestines, and supplying sufficient water to dilute the toxins and waste matter that the kidneys must excrete. After the disease has actually developed, the indications are to relieve renal congestion, to reduce the work of the kidneys as much as possible and to combat symptoms that threaten life or produce serious discomfort. Only in cases that are clearly syphilitic¹ is there any treatment that exerts a specific influence on the disease. In syphilitic nephritis, arsphenamin in doses of 3 grains (0.2 gm.), once a week, cautiously increased to 6 grains (0.4 gm.), often produces marked improvement. Mercury is, as a rule, less safe and less reliable, and should be withheld until the acute symptoms have subsided.

Absolute rest in bed is imperative in all cases and should be continued until the acute manifestations have entirely disappeared. The patient should be well covered, flannel being worn next to the skin, and great care should be taken to prevent chilling of the body.

As a rule, milk is the best food, at least for a time. It may be given alone, although usually it is advantageous to dilute it about one-third with lime-water, barley water, simple carbonated water or Vichy. When the kidneys begin to secrete more freely, cream, thin gruels, rice, milk-toast and fruit juices may be given. Beef-tea and broths must be prohibited, as they have little caloric

value and contain creatinin and other waste products which the kidneys have difficulty in excreting.

Sodium chlorid should also be withheld, especially if there is edema. Unless edema is pronounced, however, a liberal amount of water, should be allowed, as it tends to dilute the urine and to wash out cell detritus from the tubules of the kidneys. An agreeable beverage may be prepared by adding a dram (4.0 gm.) of potassium citrate, the juice of a small lemon, and a little sugar to a pint of boiling water and allowing the mixture to stand until cold. During convalescence, bread and butter, baked potatoes, and green vegetables are permissible. The return to meat proteins should be very gradual. The effect on the urine of each addition to the diet being carefully observed.

At the onset of the disease, if there is pain or suppression of urine, dry or wet cupping over the region of the kidneys is of service. Following the cupping, a hot-water bag or flax-seed poultice may be applied. Cantharides, oil of turpentine, or other cutaneous irritants should never be used. The bowels should be made to move two or three times a day, the best cathartic for the purpose usually being a saline or compound jalap powder. For children magnesia or cascara sagrada will be found sufficient. Very active purgation is not indicated unless there is extensive edema or uremia.

Free perspiration is useful in promoting elimination through the skin. It may be secured by means of hot-water baths, hot packs, vapor baths, or hot-air baths. In children hot baths and hot packs are eminently satisfactory, especially if a hot drink is administered at the same time. If the baths alone prove ineffective, their action may be supplemented by the hypodermic administration of pilocarpin in doses of from $\frac{1}{12}$ to $\frac{1}{6}$ grain (0.005–0.01 gm.), but this drug must be used with caution and only employed when necessary.

Stimulant diuretics, such as caffein, theobromin, etc., are contraindicated, but mild alkaline diuretics, such as the organic salts of potassium, often serve a useful purpose in lessening the acidity of the urine, and in removing from the renal tubules epithelial detritus and plugs of albumin. If the heart shows signs of failing, digitalis may be advantageously combined with the alkali, as in the following formula:

℞. Potassii acetatis..... ʒiii (12.0 gm.)
 Infusi digitalis..... f ʒiii (90.0 mls).—M.
 Sig.—Two teaspoonfuls, well diluted, four times a day.

When there is complete anuria, continuous enteroclysis with water or a 2 per cent. solution of sodium bicarbonate at a tem-

perature of 105° F. (40.5° C.) sometimes aids in reestablishing renal secretion.

If acute nephritis occurs early in pregnancy the uterus should be emptied as rapidly as possible; if, however, it does not develop until a late period and there are no serious symptoms (edema, retinitis, accumulation of non-coagulable nitrogen in the blood, etc.) operation may be deferred, the effects of rest, appropriate diet, etc. being carefully observed.

Decapsulation of the kidneys, first suggested by Edebohls in 1901, has occasionally proved a life-saving operation in acute nephritis. It may be considered in cases following acute infection or mercury poisoning if there is persistent anuria and symptoms of uremia are developing, and also in the kidney of pregnancy if toxic symptoms continue after the uterus has been emptied. The good effects of the operation are probably due to the relief of tension and extreme congestion.

Symptomatic Treatment.—Certain symptoms, such as extensive edema, vomiting, uremia, and anemia often require special treatment.

Edema.—If edema is marked and does not yield to restriction of liquids, removal of salt from the diet, and the purgative, diaphoretic and diuretic remedies that have already been indicated, recourse may be had to puncture of the swollen limbs, to free incision on the inner or outer side of each ankle, or the insertion beneath the skin of Southey's tubes. The last, however, should never be used unless all other measures have been found wanting. Large accumulations in the serous sacs should be removed by paracentesis.

Vomiting.—If vomiting is persistent, withdrawal of food for a time is advisable. Pieces of ice may be given to quench thirst. A mixture containing bismuth subcarbonate—10 grains (0.6 gm.) and dilute hydrocyanic acid—1 minim (0.06 mil) or a powder of cerium oxalate—10 grains (0.6 gm.) and sodium bicarbonate—5 grains (0.3 gm.) not rarely affords relief. A mustard plaster over the epigastrium may also be tried.

Insomnia.—If insomnia is sufficiently pronounced to demand the use of a somnifacient, preference should be given to bromids, chloralamid, or chloral. Trional, sulphonal and, as a rule, opiates should be avoided.

Uremia.—This complication calls for prompt and energetic treatment. The chief indications are to favor elimination of toxic metabolic products through the only available emunctories—the intestines and the skin. The bowels should be opened at once by an active cathartic, such as compound jalap powder—30–40 grains (2.0–2.5 gm.), or elaterium— $\frac{1}{6}$ grain (0.01 gm.), or,

if the patient is comatose, croton oil—2-3 drops in olive oil on the back of the tongue. Sweating should be promoted by hot-air or vapor baths. If coma or convulsions occur, or if the blood pressure is very high, venesection should be practised, the removal of from 15 to 20 ounces (450.0-600.0 mls) of blood often having a very salutary effect. In children a few ounces of blood may be abstracted from the lumbar region by means of wet cups. Unless there is marked edema, a volume of physiologic saline solution equal to that of the blood abstracted may be given subcutaneously. Whether venesection is deemed necessary or not, irrigation of the colon with a hot 2 per cent. solution of sodium bicarbonate (105° F.—40.5° C.) may be done with advantage. When stupor and coma develop without convulsions lumbar puncture is sometimes of service. If convulsions are not controlled by venesection and depurative measures, bromids or chloral may be given by the mouth or if necessary by the rectum. If these measures fail a few whiffs of chloroform may be administered by inhalation or morphin ($\frac{1}{4}$ gr.—0.016 gm.) may be given hypodermically.

During the treatment of uremia the diet should be restricted to milk.

Anemia.—After the acute symptoms have subsided iron may be employed to combat anemia. The solution of iron and ammonium acetate (Basham's mixture) is a favorite preparation but it is doubtful whether it has any advantages over other non-irritant compounds, such as ferrous carbonate or reduced iron.

Convalescence.—It is advisable to keep the patient under observation for many weeks after all symptoms of the disease have disappeared. He should be warmly clad and carefully protected from chilling. While the diet should be liberal, it should be such as will not overtax the kidneys. Over-exertion must be rigidly avoided. The skin and bowels should be kept active, the former by frequent baths and the later by saline aperients, if necessary. If the weather is cold, a temporary change of residence to a warm equable climate will be advantageous.

CHRONIC PARENCHYMATOUS NEPHRITIS

(Chronic Tubular Nephritis)

The indications are to remove the cause, if possible, to reduce the work of the kidneys by diminishing the production of nitrogenous waste and increasing the activity of the other excretory organs, to maintain the general nutrition, and to meet important

symptoms as they arise. Every patient should be carefully examined for foci of infection, and if found, these should be removed. There is ample testimony to show that the eradication of infective foci in the tonsils, teeth, or elsewhere is sometimes followed by an arrest of the disease. The patient must be guarded against vicissitudes of weather by wearing flannel next to the skin in all seasons. If he has adequate means he should be urged to spend the winter months in a warm, equable climate.

In the absence of any obtrusive symptoms, moderate exercise should be encouraged, but excessive muscular effort must be prohibited. Mental strain and worry are also injurious and should be avoided as far as possible. When the symptoms are well developed rest becomes an important factor in the treatment and much time should be passed in bed. Warm baths with friction are useful in promoting free action of the skin, but great care must be exercised after their use to prevent chilling. An occasional hot-air or vapor bath at home is often advantageous. Cold bathing should be interdicted. The bowels should be kept active, saline or other cathartics being used for the purpose, if necessary.

A great deal depends upon the diet. No hard-and-fast rules, however, can be laid down, each case being a study in itself. If there are no active symptoms, a simple nourishing diet comprising a moderate quantity of nitrogenous matter, may be allowed, its effects on the blood and urine being carefully observed. Unless there is some indication of nitrogen retention, the proteins should not be reduced below 50 grams per day.* Whatever the reduction, the remaining necessary calories must be supplied from carbohydrate and fats. Indeed, considerable caution must be exercised lest in our zeal to relieve the kidneys we reduce the strength of the patient by adhering too strictly to a low diet. The dogma that red meats are more harmful than white meats is not supported by recent investigations and should be discarded. The various forms of meats are suitable in proportion to their digestibility. Smoked meats and meat extractives should be avoided. Soups, which are unimportant as sources of energy, although usually rich in extractives, should also be excluded from the diet. Condiments, including salt, should be restricted to a minimum. Alcohol is harmful and so also is immoderate smoking.

Unless there is pronounced edema, water-drinking between meals is beneficial, and a mild alkaline mineral water, such as

* An average individual on a mixed diet consumes from 75 to 100 grams of protein per day.

Vichy or Vals may be taken to the extent of a pint (0.5 L.) or more a day.

No drugs are known that are directly curative. Iron is sometimes useful, but it is indicated only when there is actual anemia, and the indiscriminate use of Basham's mixture or of any other ferruginous preparation is to be deprecated. Myocardial insufficiency requires rest and effective digitalis therapy. A bitter, such as *nux vomica* or gentian, before meals, may be of service if there is anorexia. Vomiting is best treated by withholding food entirely for a time, and allowing only carbonated water or cracked ice. Such gastric sedatives as bismuth subcarbonate or cerium oxalate, with or without sodium bicarbonate, sometimes afford relief. Sinapisms over the epigastrium may be useful. In persistent vomiting lavage is worthy of trial. If insomnia is sufficiently pronounced to demand the use of a somnifacient, bromids, chloralamid, chloral, or barbital sodium may be tried in the order named. Opium, as a rule, should be avoided.

Edema.—Strict limitation of fluids, a rigorous salt-free diet, and rest in bed or in a chair, if the patient is orthopneic, will sometimes cause the dropsy to disappear without other treatment. The Karell diet, although it often meets with serious objections on the part of the patient, is simple and highly effective. It consists in giving 200 mls of milk at intervals of 4 hours, from 8 o'clock in the morning until 8 o'clock in the evening. No other food or liquid is allowed. If there is much thirst the patient may be permitted to rinse out his mouth with water at intervals, and if hunger is urgent a small piece of dried toast may be given with each portion of milk. If the dropsy is extensive and persistent more active dehydrating measures are required.

Purging with hydragogue cathartics, especially Epsom salt or compound jalap powder, and sweating induced by hot packs or hot-air baths are of value. Pilocarpin, owing to its depressing effects and its tendency to induce profuse bronchial secretion, should, as a rule, be avoided. Diuretics may also be of service. The best are the organic salts of potassium, theobromin, caffein, and theocin. When myocardial insufficiency is a factor digitalis is often effective, but not otherwise. The following combination, known as Grainger Stewart's mixture, may be employed:

℞. Potassii acetatis..... ʒii (8.0 gm.)
 Infusi scoparii
 Infusi digitalis..... āā fʒiii (90.0 mls).—M.
 Sig.—A tablespoonful three or four times a day.

Edema that does not yield to the remedies already mentioned may require small incisions on the inner or outer side of each

ankle or the insertion of Southey's tubes. Effusions in the serous cavities sufficient to produce functional disturbances should be removed by paracentesis.

Surgical Treatment.—In cases of chronic tubular nephritis that do not respond to the usual measures and are clearly going from bad to worse, decapsulation of the kidneys, as suggested by Edebohls, may be considered. It has not rarely prolonged life and in a few instances it seems to have brought about a complete functional recovery. The good effects of the operation have been ascribed to the relief of tension within the capsule and improvement in the renal circulation.

CHRONIC GLOMERULONEPHRITIS; CHRONIC INTERSTITIAL NEPHRITIS

The treatment in general is similar to that of chronic tubular nephritis (see p. 680). The important features are the removal of any focus of infection in the tonsils, about the teeth, in the prostate, or elsewhere or of any toxic condition that may be responsible for the nephritis, regulation of the diet, especially as regards proteins, and the avoidance of mental and physical strain, overeating, immoderate use of tobacco, chilling of the body and all other factors that may increase the blood pressure or bring about insufficiency of the myocardium.

As regards the diet, if the 'phthalein output is normal and there is no increase in the blood nitrogen, the protein intake should not be reduced below 50 or 60 grams,* as this amount is necessary in maintaining the nutrition of the body. To make up the required number of calories (2000) the amount of carbohydrate and fat food should be correspondingly increased. Except in the matter of digestibility, it makes little difference in what form of food, whether beef, mutton, chicken, fish, eggs, or beans, the protein is supplied. In marked renal insufficiency with low 'phthalein output and cumulative phenomena, the protein-bearing foods should be restricted to a minimum or for short periods withheld

* 28.3 gm. (1 oz.) of cooked *beef* yields about 6-8 gm. of protein.

28.3 gm. (1 oz.) of cooked *lamb* yields about 6 gm. of protein.

28.3 gm. (1 oz.) of cooked *chicken* yields about 6-8 gm. of protein.

28.3 gm. (1 oz.) of cooked *fish* yields about 6 gm. of protein.

28.3 gm. (1 oz.) of cooked *beans* yields about 1-2 gm. of protein.

28.3 gm. (1 oz.) of cooked *potatoes* yields about 0.6 gm. of protein.

28.3 gm. (1 oz.) of cooked *green vegetables* yields about 0.5 gm. of protein.

28.3 gm. (1 oz.) of cooked *wheat bread* yields about 2.0 gm. of protein.

28.3 gm. (1 oz.) of cooked *tapioca pudding* yields about 3.0 gm. of protein.

1 *egg* yields about 6-7 gm. of protein.

altogether. Moderation in the use of liquids is important, for the consumption of an excessive amount of fluid puts an extra burden not only upon the kidneys, but also upon the heart and blood vessels. This is one of the objections to an exclusive milk diet. Unless the disease is far advanced it is often desirable for the patient to spend the winter months in a warm, dry, equable climate. Altitudes above 1000 feet, however, should be avoided if the cardiovascular changes are at all marked.

In the treatment of the disease in its early stages drugs play but a minor role. Iron has been extensively used, but it is contraindicated unless there is actual anemia, and even then only moderate doses should be prescribed and its effects should be carefully observed. The high blood pressure is a compensatory factor enabling the kidneys to maintain adequate function. If the arterial tension is excessive it may be brought within bounds by rest, restriction of the diet, free purgation, and, if necessary, the abstraction of a few ounces of blood. Vasodilators, such as nitroglycerin and sodium nitrite, should, as a rule, be reserved for emergency and used only for short periods. If used too freely they may precipitate uremia. The occurrence of myocardial insufficiency, as shown by dyspnea on exertion, slight edema of the legs, a decrease in the day excretion of urine, etc., is to be combated by rest, the use of foods of small bulk, and the administration of digitalis in doses sufficient to produce a perceptible effect on the heart. The digitalis is indicated irrespective of the degree of arterial hypertension. Theobromin or caffeine is also of service in some cases. Severe renal insufficiency with dyspnea, restlessness and insomnia requires rest in bed or, if necessary, in a chair, and usually the use at night of some general sedative, especially chloral, 5 to 10 grains (0.3–0.6 gm.) opium, 1 grain (0.06 gm.) in suppository, or morphin, $\frac{1}{8}$ – $\frac{1}{4}$ grain (0.008–0.16 gm.) hypodermically. Occasionally, moderate doses of a bromid, alone or in combination with a nitrite, suffice. Impending uremia may sometimes be averted by complete rest, restriction of the diet to milk, free purgation, hot packs, and the use of a diuretic of the caffeine group (caffeine, theobromin or theocin). Digitalis may prove invaluable if myocardial insufficiency is a factor. The treatment of actual uremia has already been considered (see p. 679).

PYELITIS; PYELONEPHRITIS

In acute cases medical treatment consists of locating and removing, if possible, the underlying cause, in keeping the patient at rest in bed, in restricting the diet to bland, easily digestible

food, in giving an abundance of water, in securing free evacuation of the bowels, in administering urinary antiseptics or, in colon bacillus infections, sufficient alkali to render the urine definitely alkaline, and, if the infection is a stubborn one, in using auto-genous vaccines.

Hexamethylenamin is the best urinary antiseptic. It may be given in doses of 5 to 10 grains (0.3–0.6 gm.) four times a day. The efficiency of the drug depends upon the liberation of formaldehyd and this occurs only in acid urine; therefore, if the urine is alkaline it should first be made acid by the administration of acid sodium phosphate. It must be borne in mind, also, that in large doses hexamethylenamin is capable of producing hematuria. Salol is sometimes useful. It may be given alone or in combination with hexamethylenamin. In many cases of pyelonephritis due to the colon bacillus *alkalis* give better results than urinary antiseptics. Potassium citrate or potassium bicarbonate, or a mixture of the two, may be selected and given to adults in doses of 20 to 30 grains (1.3–2.0 gm.), four times a day, or to infants in doses of 10 to 20 grains (0.6–1.3 gm.) four times a day. The exact amount may be determined by testing the reaction of the urine. Not rarely success is achieved by alternating courses of hexamethylenamin and alkalis, administering each for a period of a week. In obstinate cases auto-genous vaccines should be given a trial. While they often fail, they sometimes produce marked improvement, especially in colon bacillus infections. The injections should be given every few days and the dose gradually increased from 10 million organisms to 500 million or more. In some cases after failure of internal remedies a cure has been effected by lavage of the renal pelvis with silver nitrate solution (1 : 10,000).

In pyelonephritis gravidarum it is sometimes, but not often, necessary to bring the pregnancy to an end. In pyelonephritis due to pyogenic cocci surgical intervention is often required, but it should be deferred, unless the toxemia is profound, until medical measures have had a thorough trial.

The treatment of *chronic pyelitis* resulting from renal calculus, stricture or kinking of the ureter, prostatic enlargement, etc. is largely that of the primary condition.

NEPHROLITHIASIS

(Renal Calculus)

Stones once formed in the kidney cannot be dissolved, but appropriate medical treatment may be successful in preventing the formation of fresh deposits and in flushing out small concretions. As the conditions that favor the production in excess of

uric acid, calcium oxalate, etc., and the precipitation of these substances in the pelvis of the kidney are only imperfectly understood, it is not possible to meet exactly the causal indication. However, if the urine is decidedly acid it is advisable to restrict the amount of meat in the diet and to forbid the use of foods rich in nuclein, such as liver, brain, kidney, fish roe, meat extracts, etc., as well as fancy dishes of all kinds, alcoholic beverages, and tea and coffee in excess. Irrespective of the character of the stone, much benefit often accrues from abundant water-drinking between meals. This not only favors the expulsion of small concretions, but by diluting the urine, it also tends to prevent the precipitation of the crystalloids. If the urine is highly acid the water may be made alkaline by the addition of potassium citrate—1-1½ drams (4.0-6.0 gm.) to the quart (1.0 L). As a rule, about a quart of such water should be consumed in the twenty-four hours. Some precaution is necessary not to allow the urine to become too alkaline, since this may lead to a deposition of phosphates about the primary calculus. Alkaline mineral waters, such as Carlsbad, Vichy, Vals, Contrexeville, etc., have been extensively employed, but they are less efficacious than plain water that has been rendered alkaline by the addition of potassium citrate.

Certain special remedies have been brought forward as solvents of uric acid, namely, piperazin, lycetal, piperidin tartrate and quinic acid in combination with lithium (urosin) or piperazin (sidonal). While some authorities claim to have obtained good results from these drugs, the majority of unprejudiced observers are sceptical as to their merits. Hexamethylenamin is of service in warding off infection, but it is only effective in acid urine.

Since phosphatic calculi can be deposited only from alkaline urine the indication is to render the urine acid, a task not always easy of accomplishment. Among remedies recommended for the purpose, the best are acid sodium phosphate and benzoic acid. Unfortunately the continued use of these drugs is prone to cause indigestion, an effect which detracts materially from their value.

In the milder cases of nephrolithiasis without evidence of renal infection, a sojourn at one of the well known spas, such as Carlsbad or Contrexeville on the Continent of Europe, Harrogate in England, and Bedford in America, is often beneficial, the good effects being due, however, more to the freedom of business cares and worries, the regular life and the regime than to any special ingredient of the waters.

Renal Colic.—The indications are to relax the ureteral spasm and to relieve the pain. These are best fulfilled, as a rule, by

hypodermic injections of morphin— $\frac{1}{4}$ grain (0.016 gm.) and atropin— $\frac{1}{150}$ grain (0.0004 gm.), repeated as often as necessary, the effects of the drugs being carefully observed. A hot bath (100°–110° F.) or the use of hot fomentations locally is also of service. Warm diluents should be given freely. In very severe cases inhalations of chloroform are sometimes necessary. In mild attacks benzyl benzoate in doses of 20 drops of a 20 per cent. solution by the mouth, repeated in half an hour or an hour, may suffice. After the attack the urine should be examined after every act of micturition to see if the stone appears.

Surgical Treatment.—In many cases surgical intervention affords the only hope of permanent relief. Operation is demanded when attacks of colic occur with such frequency as to prove disabling, when there are evidences of infection, and when there is persistent obstructive suppression of urine, provided, of course, that the various tests do not show such a reduction in the functional capacity of the kidneys as to render the risk of operation too hazardous. If multiple stones are present, even if the individual stones are small, and only one kidney is involved operation is usually indicated, but in bilateral nephrolithiasis, with multiple calculi, operation is, as a rule, inadvisable.

In renal calculus pyelotomy, nephrotomy or nephrectomy will be the operation of choice according to the size, shape and location of the stone, and the condition both of the affected kidney and its fellow. The operative mortality in aseptic cases is less than 5 per cent., in infected cases it is 20 per cent. or more. Owing to the great likelihood of small ureteral stones being finally passed, expectant treatment should be given a thorough trial in all uncomplicated cases. According to Braasch and Moore it is, as a rule, advisable to wait at least three months until nature has made several attempts to dislodge the stone. Kidd believes that unless there are imperative indications for operative measures it is safe to wait one or two years, as the kidney may recover sufficiently to do much useful work even if the ureter has been partially blocked for a much longer period. In large proportions of cases simple catheterization of the ureter or dilatation of the lower ureter is followed by the passage of the stone. Not rarely the injection of sterile oil or of 5 mls of 4 per cent. solution of papaverin into the ureter serves to release the calculus. Anuria unless relieved within 24 or 36 hours by hot applications to the lumbar regions, water in abundance, alkaline diuretics, intestinal irrigation with normal salt solution at 110° F., etc. demands surgical intervention.

HEMATURIA AND HEMOGLOBINURIA

Hematuria.—The treatment varies with the cause of the hematuria. If the hemorrhage is profuse, the immediate indications are to keep the patient at rest in bed, to restrict the diet to bland foods, and to reduce the concentration of the urine by allowing liberal amounts of drinking water. Epinephrin, pituitary extract, tannin, etc. are useless when administered internally. If the patient is restless and excited morphin may be given with advantage. Epinephrin solution (1:2000) may be of service in vesical hemorrhage if injected into the bladder, and also, according to Braasch, in some cases of so-called essential hematuria, if injected directly into the pelvis of the kidney. In the latter condition, if conservative measures fail and the patient's life is jeopardized by increasing anemia, recourse should be had to surgical treatment (nephrotomy, decapsulation, nephropexy, nephrectomy). Sometimes nephrotomy alone is successful, although the manner of its action is not apparent.

Hemoglobinuria.—Treatment should be directed to the primary cause. In malarial cases quinin may be used tentatively, but if its effects are unfavorable, it should be withdrawn and methylene blue (3–5 grains—0.2–0.3 gm., three or four times a day) substituted. Paroxysmal hemoglobinuria, if due to syphilis, may yield to mercury and arsphenamin. Widal has obtained good results from repeated subcutaneous injections of the patient's own blood-serum. Cold and fatigue, as far as possible, should be avoided. During the attacks the patient should be kept warm and should be given an abundance of hot liquid. Occasionally nitrites seem to have afforded relief.

DISEASES OF THE BLOOD AND HEMOPOIETIC SYSTEM

SECONDARY ANEMIA

In acute posthemorrhagic anemia the important indications are to raise the blood pressure in the medulla and to increase the volume of circulating fluid. The patient's head should be lowered and, if the loss of blood has been large, bandages should be firmly applied to all four extremities. To increase the bulk of the blood, water should be given freely and saline solution should be administered by proctoclysis, hypodermoclysis or intravenous infusion, or the transfusion of blood itself should be practised. In urgent cases, transfusion, direct or indirect, is of all measures the most effective. After the blood pressure has been restored and the acute symptoms have subsided the treatment is that of anemia from other causes.

In the treatment of chronic secondary anemia removal of the underlying cause is the chief indication. Other measures, although sometimes of service, are of secondary importance. The diet must be adapted to the digestive power of the patient. Generally speaking, it should be abundant, varied and nutritious. Meat, eggs, fat, green vegetables and milk are indicated. An abundance of fresh air, frequent bathing followed by vigorous friction of the skin, massage, an amount of physical exercise adjusted to the patient's strength and primary disease, and change of scene are all important aids in treatment. Of drugs, none is so generally useful as iron, which in many cases is best given in the form of Bland's pill, 5 grains (0.3 gm.) after each meal for a week, and then, if necessary, 10 grains (0.6 gm.) at the same intervals. Reduced iron and Basham's mixture are also reliable preparations. In cases with marked gastric disturbance citrate of iron may be given by intramuscular injection. Ampules containing 3 grains (0.2 gm.) of the drug in sterile solution are on the market and the contents of one of these may be injected every other day. Arsenic is often a useful adjuvant to iron. Fowler's solution may be chosen as the preparation and given in gradually increasing doses to the point of toleration. If arsenic is not well borne when given by the mouth it may be administered by intramuscular injection in the form of sodium cacodylate— $\frac{1}{2}$ grain (0.03 gram) daily, gradually increased to 2 grains (0.13 gram) daily.

In severe cases intravenous injections of arsphenamin are sometimes effective, even in the absence of syphilis. Reactions to the drug, however, must be avoided. In secondary anemia with a very low percentage of hemoglobin transfusion of blood may also result in marked improvement. Bitters, such as nuxvomica and gentian, are frequently useful in combating anorexia arising from anemia. To secure the best results they should be given in liquid form about half an hour before meals.

CHLOROSIS

An abundance of sunlight and fresh air, a diet of simple but nourishing food, and, in all but the mildest cases, rest in bed for two or three weeks will do much to hasten recovery. Daily evacuation of the bowels should be procured by regulation of the diet and if necessary by the use of laxatives, of which the best, perhaps, are cascara sagrada, rhubarb, aloes and phenolphthalein.

The specific remedy for the disease is iron, but how this drug exerts its beneficial influence is not known. According to Morawitz, it probably acts not so much upon the bone-marrow as upon the basic cause of chlorosis, which seems to be a distur-

bance of the secretions of the ductless glands. One of the most satisfactory preparations of iron is Blaud's pill, one 5-grain (0.3 gm.) pill being given after each meal during the first week, two pills after each meal during the second week, and three pills after each meal thereafter, the treatment being continued for several weeks after the hemoglobin has reached the normal amount. Other reliable preparations of iron are reduced iron, the citrate of iron and the pyrophosphate of iron. If for any reason iron cannot be taken by the mouth, the citrate of iron may be given by intramuscular injection. (See page 303.) Arsenic in the form of Fowler's solution, 5 minims (0.3 mil), three times a day, or arsenic trioxid, $\frac{1}{40}$ grain (0.0016 gm.), three times a day, is sometimes a useful adjuvant to iron. If there is anorexia a bitter stomachic, such as *nux vomica* or *gentian*, should be given before meals.

PERNICIOUS ANEMIA

Rest is beneficial and during exacerbations it is imperative. An abundance of fresh air and sunshine is important. The diet should be liberal and should consist of nutritious and easily assimilable food, the amount and particular kind being adjusted to the digestive power of the patient. With the view of increasing the bulk of the blood it is sometimes advisable to reinforce the diet with an abundance of milk. Gentle massage is useful, especially when prolonged rest is required. The bowels should be evacuated daily, using for the purpose, if necessary, suitable cathartics or preferably colonic irrigation with salt solution. Focal infection should be sought for in the teeth, gums, nose, paranasal, sinuses, urogenital tract, etc., and if found an attempt should be made to remove it, since even if it is not the sole cause of the disease, it may at least be an accessory factor.

As regards special remedies, the reputation of arsenic seems to be well founded. This drug may be administered in the form of Fowler's solution, beginning with 3 minims (0.2 mil) three times a day after meals, and increasing 1 minim (0.06 mil) daily until 15 minims (1.0 mil) per dose are taken, provided no symptoms of saturation appear. After continuing for a week with full doses, the drug should be discontinued for several days and then resumed, beginning with one-half the maximum dose and increasing the amount by increments as before. If the arsenic cannot be taken by the mouth, it may be given in the form of sodium cacodylate by intramuscular injection, using 2 grains (0.13 gm.) once daily for a week and then intermitting the treatment for a week. Arsphenamin has been used with gratifying results in

some cases (Bramwell, Boggs, Lampe and others), but its effects are not always good and it is inadvisable to employ it if the hemoglobin is below 25 per cent., as the drug itself causes temporary hemolysis. Iron is either useless or actually deleterious. On account of the gastric anacidity the use of diluted hydrochloric acid in large doses has had many advocates.

If the anemia still progresses and the blood regenerative power seems to be incapable of stimulation by the usual methods, transfusion of fresh unmodified blood that is compatible with that of the patient often proves more effective than any other measure. From 250 to 700 mls may be injected at intervals of a week to a month. If untested blood is employed the first 100 mls should be introduced into the vein very slowly, and the transfusion immediately suspended if untoward symptoms (sensation of tingling in the limbs and of oppression about the precordium, cyanosis and embarrassed respiration) develop. Generally speaking, the earlier transfusion is performed, the better are the results. The measure, however, is never curative and with frequent repetition gradually loses its efficiency.

Finally, in selected cases splenectomy seems to be advisable although it has never proved more than a temporizing procedure. The best results have been observed in comparatively young patients in whom the spleen is moderately enlarged and the blood condition is fairly good, notwithstanding a considerable degree of hemolysis, as shown by high values for blood-derived pigments in the duodenal contents or the stools. The operation is contraindicated by spinal cord symptoms and a count of red cells below 1,500,000, especially if this is associated with signs of bone-marrow exhaustion (absence of erythroblasts, absence of reticulated cells, low percentage of polymorphonuclear leukocytes, etc.). When the anemia is severe several transfusions should be performed as a preliminary measure. Transfusion may also prove useful in case of relapse after operation. The most favorable report on splenectomy is that from the Mayo Clinic, which is based upon 50 cases. The operative mortality was 6 per cent. Of the patients who recovered from operation, 21.3 lived 3 years or longer and 10.6 per cent. survived $4\frac{1}{2}$ years or longer and at the time of the report were still living. The conclusion is that splenectomy prolonged life in at least 20 per cent. of the cases.

LEUKEMIA

Chronic Myeloid Leukemia.—An effort should be made to maintain the general nutrition by regulating the diet and attending to hygienic measures. Rest is helpful. Among drugs,

chemically pure benzol often produces marked temporary improvement, although it is by no means free from dangerous toxic properties, and it not rarely produces unpleasant symptoms, such as nausea and vomiting, headache and dizziness. It is best given in capsules with an equal amount of olive oil, the dose being cautiously increased from 10 minims (0.6 mil) to 20 minims (1.2 mils) three times a day. During the treatment the patient should be at rest, preferably in a hospital, and blood-counts should be made at frequent intervals. When the leukocytes have been reduced to 25,000 per cubic millimeter the administration of the benzol should be immediately suspended. Persistent headache, evidences of renal irritation, increasing anemia or even a very rapid fall in the leukocyte count should also be the signal for withdrawal of the drug. Pushed too far, the use of benzol may result in total atrophy of the hemogenetic tissue. Arsenic in doses gradually increased to the point of toleration is also of service, especially when the red-cells and hemoglobin are diminishing. If the stomach is intolerant intramuscular injections of sodium cacodylate, in doses of 2 grains (0.13 gm.) every other day, may be substituted for arsenic by the mouth.

Of all therapeutic agents, however, the roentgen ray is the most generally useful. Skillfully applied, with its effects controlled by repeated blood examinations, it may suppress all symptoms of the disease for months, although it never alters the final result. As Stengel and Pancoast have shown, the best results are achieved when the ray is applied to the bones, various portions of the body being treated in succession, and the spleen not exposed until it is reduced considerably in size and the patient's general condition is much improved, and even then only with caution. Radium sometimes succeeds in cases which prove refractory to the x-ray. Radiotherapy may sometimes be combined advantageously with the benzol treatment. Splenectomy is rarely advisable, although Giffin of the Mayo Clinic reports encouraging results in at least 6 of 26 cases in which operation was performed after the blood-picture was brought to normal by the use of radium, x-ray, or benzol.

Chronic Lymphoid Leukemia.—The treatment of chronic lymphoid leukemia is virtually that of chronic myeloid leukemia, although, as a rule, the former will be found to be less readily influenced both by radiation with the x-ray or radium and by benzol therapy.

Acute Leukemia.—There is no known effective treatment. Injections of normal horse serum and transfusion of blood have been tried, but without favorable results. The use of the roentgen ray is contraindicated.

HODGKIN'S DISEASE

Treatment by x-rays or radium emanations, directed not only to the palpable lymph-nodes, but to all the lymphoid structures of the body, including the mediastinal and abdominal nodes, often produces marked improvement, but is never curative. Tates and Bunting recommended as a preliminary measure the elimination of all possible foci of infection, such as may exist in the tonsils, teeth, etc., and, after this has been accomplished, the complete extirpation of all affected lymphoid tissue accessible to the knife, with postoperative radiation and the use of an immune serum prepared with the diphtheroid organism often found in the lesions. With this plan of treatment, they believe that a cure may be obtained in about 20 per cent. of all cases. Other writers of large experience, however, are not so optimistic about operative measures, although they do not deny the possibility that complete excision, if undertaken when the process is confined to a single focus, and followed by radiotherapy, may occasionally prove curative. As to drugs, arsenic in the form of Fowler's solution by the mouth or of arsphenamin by intravenous injection, is sometimes of definite value, but it is without specific or lasting effect. The hygienic and dietetic treatment of the disease is that of simple anemia.

ERYTHREMIA

(Vaquez's Disease, Polycythemia Vera)

Venesection often affords relief, but its good effects are only temporary. X-ray or radium treatment of the bones has been of benefit in some cases. In four or five instances no return of the symptoms was observed up to 5 years following the treatment (Béclère). Pendergrass and Pancoast recommend giving inhibitory doses of the roentgen ray to the long bones, with the view of inhibiting the formation of red cells, and stimulating doses over the spleen with the view of increasing the normal function of that organ.

In two of Turck's cases Fowler's solution (30 drops daily) was apparently beneficial. Benzol has been recommended, but its effects have not been satisfactory. Splenectomy has not produced favorable results, indeed it is likely that the splenomegaly is a compensatory condition. A restricted diet, hydrotherapy, repeated bleeding and courses of bromids relieve the nervous symptoms.

HEMOPHILIA

Members of bleeder families, particularly female members, should be advised not to marry. Hemophilic children should be placed under good hygienic conditions and should be protected, so far as possible, from traumas of all kinds. No operations on them, not even trivial ones, should be undertaken, except for conditions that in themselves may prove fatal. Vaccination by sarification, however, may be performed without misgivings. Residence in a warm climate, especially during the winter, is advisable.

When bleeding occurs rest, compression, and applications of epinephrin, gelatin, tannin, or ice may be tried, although they will usually be found ineffectual. Calcium salts are frequently employed internally, but are rarely of benefit. The best results are obtained from the use of serums or applications of fresh tissues or extracts of tissues, such as brain, thyroid gland, spleen, etc. Serum may be administered intravenously or subcutaneously or applied locally to the bleeding point. Human serum, if it can be obtained, is preferable, but horse serum, even in the form of diphtheritic antitoxin, or rabbit serum, may be used. The usual dose for intravenous injection is from 20 to 30 mils, repeated daily if necessary. Thromboplastin in the form of an extract of brain (kephalin) or an extract of blood-platelets (coagulen), applied locally to bleeding wounds, has been found effective. In very obstinate cases the indications are best met by blood transfusion (100 to 500 mils). Unmodified blood is preferable, but before it is transfused, tests for agglutination and hemolysis, and for syphilis should, of course, be made.

Recent hemarthrosis should be treated by rest and moderate compression, or, if the effusion is large, by aspiration with a fine needle, followed by the application of a pressure bandage. After several days gentle massage is indicated.

PRIMARY PURPURA

Mild forms of the disease require no special treatment. In severe cases rest in bed is of prime importance. Many remedies have been recommended, but only a few are worthy of consideration. In some instances oil of turpentine seems to be of service. Calcium chlorid, 20 grains (1.3 gm.), three times a day, has been extensively used on the advice of Sir Almroth Wright, but there is no evidence that it is of value unless the hemorrhagic tendency is due to a lack of available calcium in the blood, and this appears to be the case only in obstructive jaundice. Subcutaneous injections of fresh blood serum, 30 mils daily, although favorably

reported upon by some clinicians, is usually of little avail. The best results are secured by the transfusion of whole blood, which contains all the elements concerned in clotting. In many cases this measure brings about a prompt cessation of the bleeding.

Of local hemostatic remedies, the best, perhaps, are kephalin, an extract of brain tissue, and coagulen, an extract of blood platelets, both of which are rich in thromboplastin. The intravenous use of these agents has also been proposed, but it is by no means devoid of danger. Coagulen (5 gm. in 300 mls of saline solution), however, may be safely given subcutaneously. Stephan reports a case of purpura fulminans which was successfully combated by means of deep roentgenotherapy applied to the spleen.

HEMOLYTIC JAUNDICE WITH SPLENOMEGALY

The persistent use of iron seems to have been of service in some cases of the acquired form, but the drug is useless in the congenital type. Roentgen-ray treatment has been beneficial in some cases. If the disease causes much inconvenience splenectomy should be considered, but the operation should be avoided during a crisis. Elliott and Kavel report that of 48 cases subjected to operation death occurred in only 2. In the other 46 the symptoms virtually disappeared. Giffin, of the Mayo Clinic, reports 12 cases treated by splenectomy, with 1 operative death and 1 death 4 months after operation. Of the 10 patients who survived the operation 9 were in excellent health at the time of the report and 1, who had had a relapse after 2 years, was in fairly good health, following two transfusions.

SPLENIC ANEMIA; BANTI'S DISEASE

If there is a suspicion of syphilis energetic antisyphilitic treatment should be instituted, although too much should not be expected from it. Iron and arsenic are virtually without effect. Indeed, splenectomy, as originally advocated by Banti, is the only measure that offers any chance of permanent benefit. If done in the first or second stage, the operation is not only attended by a comparatively low mortality (10 to 15 per cent.), but in the large majority of cases is followed by a cure or great and lasting improvement. In the third stage, with permanent changes in the liver splenectomy is much more dangerous (mortality, 25 to 50 per cent.) and is much less likely to be of benefit, although even at this late period it has been more or less successful in some instances. A combination of splenectomy and Talma's operation has been recommended for advanced cases

DISEASES OF THE DUCTLESS GLANDS

SIMPLE OR NON-TOXIC GOITER

Iodin is of value in both prophylaxis and treatment. It has been shown that 30 grains (2.0 gm.) of sodium iodid, taken in doses of 3 grains (0.2 gm.) for 10 days, twice yearly, is not only effective in reducing simple thyroid enlargements, but in preventing them. Overuse of the drug must be avoided, as there is some danger, especially in persons more than 40, of transforming an atoxic goiter into a toxic one. Marine and Kimball showed that among 2190 normal girls under prophylactic treatment annually only 5 showed any enlargement of the thyroid; while of 2305 normal girls not taking iodine, 495 showed enlargement. One-third of the simple goiters disappeared or were markedly improved under iodine.

In early cases applications of iodine in the form of the tincture or of an ointment of cadmium iodid—20 grains to the ounce (1.3 gm. to 30.0 gm.)—is sometimes of service. X-ray has also been used with some success. Large and growing goiters, and especially those producing toxic symptoms, should be treated surgically.

EXOPHTHALMIC GOITER

(Graves' Disease)

The treatment aims at lessening the excitability of the nervous system and diminishing the output of the thyroid secretion. Rest of body and mind is absolutely essential. Even in mild cases the rule should be 2 or 3 weeks of complete rest in bed, and after this period at least 10 hours of rest at night with an additional hour or two during the day. In severe cases and during acute exacerbations of less severe cases the period of complete rest should be from 4 to 6 weeks or even longer. As much time as possible should be spent in the open air. Freedom from worry and excitement of all kinds is no less an important element of the treatment than exemption from physical exertion. The rest is effective not only in restoring nervous control but also in securing a marked reduction in metabolism. Psychotherapy and suggestion are not without influence; indeed, it is likely that good effects have sometimes been ascribed to remedies that in reality were due not to the remedies themselves but to a powerful mental impression created in administering them. The diet should be abundant and nutritious, but at the same time plain and unstimulating and restricted somewhat in respect of meats. Highly seasoned dishes, tea, coffee and alcohol

are, as a rule, inadmissible. If there is much loss of weight it is usually advisable to give milk between meals or on retiring. When the patient is able to be up and about a change of scene and air often proves beneficial. High altitudes should be avoided if cardiac weakness is pronounced and no place should be chosen in which the patient cannot secure good food and mental tranquility. Sea-bathing must be forbidden. Massage and general hydrotherapeutic measures, judiciously employed, may be of service. It is doubtful, however, whether the various forms of electrotherapy have more than a suggestive influence, although stabile galvanism of the cervical sympathetic has had the approval of many clinicians of large experience. The application of x-rays to the thyroid and thymus glands has in some cases proved to be of much value.

Many drugs have been highly praised from time to time, but none appears to have any influence on the fundamental process. Iron and arsenic are useful in anemic subjects. If nervous excitability and restlessness are pronounced potassium or sodium bromid in doses of 20 or 30 grains (1.3–2.0 gm.) at bedtime may be given with advantage. Tachycardia and palpitation are best treated by rest and the application of an ice-bag to the precordium. Belladonna given to the point of tolerance is sometimes of service, but the manner of its action is not known. Digitalis may be useful if there are evidences of cardiac dilatation, otherwise it is likely to fail. Laxative remedies are often beneficial and it is probable that sodium phosphate, which in doses of 15 to 20 grains (1.0–1.3 gm.) three times a day, has given good results in the hands of some observers, owes its virtues to its action on the bowels. Diarrhea, which is often refractory, is best treated, as a rule, by rest in bed, liquid diet, and the administration of bismuth subcarbonate and tannalbin. In some cases hydrochloric acid by relieving achylia acts well. Persistent vomiting may require the use of morphin hypodermically. The employment of special antitoxic and cytolytic preparations (serum of thyroidectomized animals, milk of thyroidectomized goats, cytolytic serum of Beebe and Rogers, and etc.) has proved disappointing. Thymus extract is useless and thyroid extract and iodids are, as a rule, harmful.

While many patients can be cured or much benefited by well-directed medical measures, surgical intervention offers by far the greater chance of success, and for this reason is to be recommended after medical treatment has been given a fair trial or at once if the patient's circumstances are such as to render impracticable a prolonged period of rest. Operation should not be done during acute exacerbations or crises or in cases far advanced with

extensive degeneration of the cardiac muscle. Auricular fibrillation is not in itself a contraindication to surgical intervention, although it adds, of course, considerably to the danger. As regards the form of operation, each case presents its own problem as to whether it should be treated by boiling water injections, by ligation of one or more of the thyroid arteries, or by partial thyroidectomy. In skillful hands the mortality of thyroidectomy is at present not above 2 or 3 per cent. Crile under a plan of treatment that included the adoption of nitrous oxid-oxygen, the use of local anesthesia, the multiple stage operation, and the exclusion of the psychic factor, had but 2 deaths (1.1 per cent.) in a series of 182 consecutive thyroidectomies. After operation medical supervision is always necessary for several years at least.

SECONDARY HYPERTHYROIDISM; TOXIC GOITER

The medical treatment is that of exophthalmic goiter. Local sources of infection should be sought for and, if possible, removed. Prolonged rest and x-ray treatment are valuable and sometimes results in a permanent cure. Surgical intervention is always indicated when well-directed medical treatment fails to produce any definite or lasting improvement. As a rule, the operation should be directed at once to removal of the tumor. Preliminary ligation is rarely of benefit. The relief afforded by surgical treatment occurs earlier and is more complete in toxic goiter than in exophthalmic goiter. Even after the occurrence of auricular fibrillation marked improvement is sometimes noted.

HYPOTHYROIDISM; MYXEDEMA

As patients with myxedema are very susceptible to low temperatures, they should be warmly clad and protected from cold. Residence during the winter in a warm sunny climate is desirable. Warm baths are beneficial. It is important to keep the bowels regular. The essential element of treatment, however, is the more or less continuous administration throughout life of an extract of animal thyroid glands or of the thyroid hormone, thyroxin. The implantation of thyroid tissue has rarely, if ever, been successful. The most suitable dose of thyroid extract must be determined by trial in each case. It is best to begin with a small dose—2 grains (0.13 gm.) of the dried gland a day—and to increase the amount every two or three days until the symptoms begin to disappear. Usually the maximum dose of 10 to 15 grains (0.6–1.0 gm.) daily may be reached within a fortnight, and during this period if the patient shows any

indications of cardiac or arterial degeneration, it is advisable for him to remain in bed. Once the full therapeutic effect of the drug has been secured, it may be maintained by smaller doses, often 5 grains (0.3 gm.) once a day, or even every second or third day, being sufficient for the purpose. Larger doses are required in winter than in summer. In all cases the dosage must be carefully supervised, as alarming symptoms sometimes develop suddenly. Dyspnea, tachycardia, vomiting or purging, marked prostration, or anginoid pains should lead to the immediate suspension of the treatment for the time. According to Plummer, there are approximately 10 mg. of thyroxin in 150 grams of desiccated thyroid, and a daily oral dose of 1.6 mg. of thyroxin will hold the basal metabolism of most thyroidless individuals within normal limits. As a rule, if thyroid medication is instituted early, before the occurrence of serious degenerative changes in the vascular system and kidneys, the symptoms entirely disappear and the patient remains well as long as the treatment is continued.

In *cretinism*, also, marvellous results are frequently achieved by thyroid medication, especially if it is begun early. In many cases, however, mental improvement, though marked, does not keep pace with bodily growth, and a complete cure is somewhat exceptional. Indeed, in severe endemic cretinism the patient, despite specific treatment, not rarely remains wholly idiotic.

ADDISON'S DISEASE

Adrenal preparations have been given with benefit in some cases, but on the whole the results have not been satisfactory. From 10 to 20 grains (0.6–1.3 gm.) of the dried extract of the gland may be given by the mouth three times a day. Epinephrin has also been used subcutaneously, but its value is even more doubtful than that of the extract, as there is little evidence that suprarenal insufficiency is the result of a loss of epinephrin function.

Apart from organotherapy, the chief indication is to conserve in every way the patient's strength. Rest is necessary and should be more or less complete according to the degree of adynamia. The diet should consist of nutritious, easily digestible food. Tonics, especially strychnin, arsenic and iron, are sometimes useful. To combat vomiting, carbonated water, champagne, cerium oxalate, bismuth subcarbonate and diluted hydrocyanic acid should be tried. Sinapisms over the stomach may be of service. Grawitz found gastric lavage effective in two cases. Strong purgatives are inadmissible as they may excite a persistent diarrhea or cause fatal syncope.

ACROMEGALY

Thyroid extract persistently used is occasionally of value, especially in relieving headache and improving vision. Extract of the pituitary gland seems to have been of service in some cases, particularly after the occurrence of symptoms suggesting hypopituitarism. An extract of the whole gland may be tried and if this fails an extract of the posterior lobe may be substituted. The dosage must be determined by studying the effects of the drug. Mercurial inunctions have been followed by improvement in two or three instances. If the local symptoms are severe one of two surgical operations—decompression or hypophysectomy—may afford relief. Cushing reports 190 operative cases of pituitary disease, only a few of which, however, were acromegalias, with a mortality of 9.7 per cent. when the transphenoidal route was selected and a mortality of 7.5 per cent. when the transfrontal route was selected. In Adson's series of 20 cases there were 6 deaths.

HYPOPITUITARISM

In all forms of hypopituitarism both pituitary extract and thyroid extract are worthy of trial. In a number of instances good results have been obtained from one or the other of these remedies. If there is severe headache or failing vision surgical measures (decompression or removal of the growth) should be considered.

STATUS LYMPHATICUS

General hygienic measures that will tend to improve the patient's nutrition and increase the resistance to infection are indicated. Rickets, if present, should be carefully treated. Emotional excitement, excessive physical exertion, cold bathing, surgical operations, and all other provocatives of attacks should be avoided. During attacks the child should be kept in a horizontal position, warm applications should be made to the neck, and cardiac stimulants should be given, if necessary. Unless relief is afforded, intubation with a long tube should be practised. The x-ray may be of service in reducing the size of thymus. In a number of cases of thymic enlargement with pressure symptoms, operation (complete or partial thymectomy, decompression by resection of the manubrium, elevating and suturing) has given good results. According to DaCosta, in 42 reported cases of thymectomy there were 15 deaths.

DISEASES OF THE JOINTS, BONES AND MUSCLES

ARTHRITIS DEFORMANS

The chief indications are to get rid of the original focus or foci of infection, to increase the patient's powers of resistance, to relieve pain, and to secure the maximum amount of efficiency in the affected joints. In searching for primary sources of infection it is often necessary to enlist the services of a skilled dentist, roentgenologist, rhinologist or genito-urinary surgeon. So far as the teeth are concerned, it must be borne in mind that alveolar abscesses may be present without producing pain or any changes in the mouth that are evident on ordinary inspection. X-ray examination is usually necessary, but interpretation of the findings requires much experience and good judgment. Removal of teeth is justifiable only when there are definite indications of deep-seated infection.

The diet should consist of easily assimilable food and, as a rule, should be liberal. In some cases, however, especially when no infective foci can be found or when infective foci have been removed without benefit to the patient, a reduction of the intake of carbohydrate and protein food below the level of which the patient has been accustomed may yield satisfactory results. If the patient is well nourished or obese the intake of food may sometimes be reduced as much as 1000 calories with advantage. To guard against too great a loss of weight, the carbohydrates and proteins that have been withdrawn from the diet may be replaced in part by fats—butter, cream, olive oil, codliver oil. Of course, severe dietetic restrictions are out of place if the patient is already anemic and emaciated.

General hygienic measures are of great importance. The patient must be warmly clothed, must have his bowels open at least once daily, must keep his skin active by frequent bathing, must take water freely, and must be protected from wet and sudden changes of temperature. A change of climate, especially in cases that are not far advanced, frequently exerts a favorable influence. Visits to hot mineral springs (Hot Springs of Virginia or Arkansas, Bath, Baden-Baden) are often helpful. Residence in a dry, warm climate—Southern California, Arizona, Riviera, Egypt—particularly during the changeable seasons, may in itself be productive of much good.

A cheerful environment, with an abundance of sunshine and fresh air, and hydrotherapy, particularly in the form of an alternating hot and cold douche or spray applied to the spine with considerable force for a few minutes every other day or every day, are valuable adjuvants to other therapeutic measures.

Absolute rest is necessary in every case as long as motion causes pain.

The most generally useful drugs are the syrup of ferrous iodid and arsenous acid. The former may be given in doses of 20 to 30 minims (1.2–2.0 mls) and the latter in doses of $\frac{1}{60}$ to $\frac{1}{40}$ grain (0.001–0.0016 gm.), three times a day after meals. Endocrine therapy is beneficial in some cases. Thymus extract (5–10 gr.—0.3–0.6 gm.), pituitary extract (5 gr.—0.3 gm. of the whole gland), or thyroid extract (1–2 gr.—0.06–0.13 gm.) three times a day, may be tried, but the effects of the last must be carefully observed.

Vaccines, especially if autogenous, are of real value during the more acute stages of the disease in a small proportion of cases, but they must never be used as a substitute for the removal of the causative infection if this can be located and its eradication is feasible. The dose is 10 million killed microorganisms, increased, if necessary, to 2 billion, every 4 to 7 days. The intravenous injection of a non-specific protein antigen, although sometimes productive of severe reactions, is on the whole, as effective as specific bacterial vaccination. Killed typhoid bacilli may be used for the purpose, the dose being 75 million to 200 million every two or three days, or in rare instances as often as once a day. Eidelsberg reports good results from intramuscular injections of milk that has been heated in a closed vessel at 100° C. (in boiling water) for 20 minutes. The injections were made into the buttock at intervals of from 3 to 7 days, and the dose was 4 to 5 mls for the first injection, 5 to 8 mls for the second, and from 7 to 10 mls for the third, fourth and fifth injection. A moderate reaction was necessary to obtain an improvement. Salicylates and phenyleinchoninic acid (atophan) are useful as analgesics, but have no influence on the disease itself. General tonics, especially iron and nux vomica, are frequently required in anemic and emaciated patients. Cod-liver oil, in such doses as the stomach will tolerate, may also be of service, if there is much malnutrition.

OSTEOMALACIA

A good hygienic environment, an abundant nutritious diet, the termination of lactation, and the avoidance of pregnancy are important indications. Medicinal treatment is empiric. Phosphorus and epinephrin have been efficacious in some cases. Phosphorus is best given in pill form and in doses of $\frac{1}{100}$ grain (0.00065 gm.) three times a day, over several months. Epinephrin is given subcutaneously in doses of 0.5 to 1.0 mil of the

1:1000 solution, once daily, for three or four months. Castration, originally suggested by Porro, has many successes to its credit, and is advisable when other measures fail. Whether it acts by removing some baneful influence of the ovaries themselves or solely by the prevention of pregnancy is debatable. According to Schnell recovery occurred in 98 to 105 cases treated by castration and in 12 of 32 cases treated by epinephrin. Sterilization by roentgen rays has proved beneficial.

LUMBAGO

The treatment varies with the cause. In acute cases anodynes are required. A combination of acetylsalicylic acid and acetphenetidin often suffices. Occasionally it may be necessary to resort to morphin. Locally, heat, support by straps, friction with methyl salicylate or irritating liniments, or dry cupping almost always affords great comfort. An excellent method in many cases is to rub the part thoroughly with methyl salicylate, cover it with flannel, and then pass over it several times a heated flat-iron. In refractory cases mustard plasters, flying blisters, or light applications of the Paquelin cautery should be tried. Free sweating is sometimes useful. In chronic lumbago treatment must be addressed to the underlying condition. Cases due to sprain, arthritis or sacroiliac relaxation will require immobilization of the parts by straps of adhesive plaster or specially constructed corsets. Unilateral defects in balance are sometimes corrected by elevating one heel. Lumbago due to a pendent abdomen is usually relieved by a close-fitting supporter or corset. In septic cases the primary source of the infection must be removed. Backache resulting from relaxed muscles and postural curve will be benefited by the assumption of a correct standing and sitting position, gymnastic exercises, massage, shoulder-straps, etc. In severe cases, irrespective of the cause, recumbency for a part of the day is often necessary at first.

PROGRESSIVE MUSCULAR DYSTROPHY

(Primary Myopathy)

Avoidance of fatigue, hydrotherapy, massage, electric procedures, and the administration of tonics, especially strychnin, may retard the progress of the disease but never arrest it. Extracts of the adrenal, pituitary, and thymus glands seem to have been of service in some cases.

MYASTHENIA GRAVIS

Treatment is unsatisfactory. Rest of body and mind, careful feeding, and the avoidance of cold are of most importance. If the symptoms are severe the patient should be confined to bed. Electricity, especially, faradism, is contraindicated. Massage is useless. Strychnin has been employed, but not often with benefit, although Dana reports good results from the drug when given hypodermically in doses cautiously increased to $\frac{1}{4}$ grain (0.016 gm.) once a day or even twice a day. In individual cases improvement has followed the use of pituitary and ovarian extract (Delille and Vincent), adrenal extract (Sicard, Dufour), thymus extract (Goodhart), calcium lactate (Spiller), and roentgen-ray treatment of the thymus (E. W. Taylor).

DISEASES OF THE NERVOUS SYSTEM

NEURITIS

Removal of the cause, if possible, and absolute rest of the affected part are the first requisites of treatment. When the nerves of the limbs are involved it may be necessary to use splints and bandages to prevent muscular action. Moist heat in the form of compresses or of local hot baths is often beneficial. Occasionally, cold applications are more effective. A saturated solution of magnesium sulphate on several thicknesses of gauze may be used. In less acute cases counterirritation by means of small blisters or the Paquelin cautery at points where the nerve-trunk is especially tender sometimes affords relief. In mild forms of the disease ointments of belladonna and methyl-salicylate may suffice. When the pain is very persistent exposure of the part to superheated air in a Tallermann apparatus may have a good effect. Of the analgesics, the coal-tar derivatives, acetphenetidin and the salicylates, are, as a rule, the most useful. A combination of these drugs with codein is especially efficacious.

℞. Acetphenetidini..... ʒi (4.0 gm.)
 Acidi acetylsalicylici..... ʒiiss (6.0 gm.)
 Codeinæ sulphatis..... gr. iiii (0.2 gm.).—M.
 Ft. chart. No. xii.
 Sig.—One every three or four hours.

Morphin should be used only as a last resort. After the symptoms of irritation have completely subsided the indications are to maintain nutrition in the paralyzed muscles by systematic massage and electrical treatment and to prevent contracture in the muscles and stiffness of the joints by passive movements.

When faradic contractility is lost, which is frequently the case, labile or interrupted galvanic currents should be employed with that pole applied to the muscles which gives the better contractions. In traumatic cases which show no tendency to recover after several months, surgical intervention (removal of cicatricial tissue with suture of the divided nerves, nerve anastomosis, or tendon transplantation) should be considered.

Multiple Neuritis.—Careful search should be made for the exciting cause with the view of removing it, if possible. In all cases, except mild forms involving only the arms, rest in bed is essential and if the pain is severe a water-bed is desirable. To avoid shortening of the calf muscles, the legs, so far as possible, should be kept extended, and to prevent foot-drop, the pressure of the bed-clothes should be removed by wire hoops and the soles supported by pillows or sand-bags. The diet must be abundant and nutritious, but easily digestible. The pain is often relieved by warm fomentations or gentle friction with warm oil. Occasionally, however, cold applications afford more comfort. Such drugs as acetphenetidin and the salicylates are usually required, but they must not be used continuously on account of their depressant effects. In some cases the pain is so intense that morphin must be employed.

In the chronic stage warm baths, massage, electricity, passive movements, and educational gymnastics are the measures to be employed in promoting the nutrition of the affected muscles aiding in the repair of the damaged nerves. Tonics, especially strychnin and iron, are also of value. Convalescence is often hastened by a change of air and scene. In long-standing cases with contractures and deformities surgical intervention may be necessary.

SCIATICA

The cause must be removed, if possible. In all cases rest is essential. If the symptoms are severe not only should the patient be put to bed, but the movements of the affected limb should be restricted by sand-bags or a long hip splint. Free evacuation of the bowels should be secured in order to deplete the pelvic veins. Irrespective of the cause of the disease, such drugs as the salicylates, acetphenetidin, and cinchophen (atophan) in full doses are sometimes effective in relieving pain. Morphin is sometimes necessary, but it should be used only as a last resort. Counterirritation is sometimes of service. It is best accomplished by means of dry cups or small blisters along the course of the nerve. In some cases acupuncture acts satisfactorily

and in others good results are achieved by directing a stream of hot water down the back of the thigh. High frequency electric currents or static induced currents are sometimes very effective. Massage is contraindicated.

In refractory cases, when no organic abnormalities outside the sciatic nerve are discoverable, injections of normal salt solution into the tissues surrounding the nerve or into epidural space are worthy of trial. Complete or partial relief, often lasting, may be expected in at least one-third of the cases. In perineural injections the fluid (100 to 150 mils) is introduced forcibly at a point 1 inch to the outer side of the junction of the inner one-third and the outer two-thirds of a line drawn from the sacro-coccygeal articulation to the lowest point of the postero-external border of the great trochanter, the needle being inserted directly downward through the gluteal muscles until the nerve is reached (6-12 cm.), as shown by a sharp, shooting pain down the leg. Owing to their destructive action, injections of alcohol are contraindicated. Epidural injections (50 to 80 mils of salt solution, the first with epinephrin and novocain) are made at the level of the sacro-coccygeal articulation through the foramen sacrale superius.*

Arthritic cases will require removal of the infective focus, if this can be discovered, and appropriate orthopedic measures. Cases due to prostatitis or spermatoecystitis may require the aid of the genito-urinary surgeon. Finally, when sciatica exists without obvious cause and medical treatment proves ineffectual, the nerve should be exposed by an incision and examined for adhesions. The operation entails but little risk and offers a very considerable chance of permanent relief. Nerve stretching occasionally does good, but in the large majority of cases it fails.

NEURALGIA

An effort should be made to adapt the treatment to the etiology of the disease. Causes of peripheral irritation, such as dental caries, impacted teeth, inflammation of the accessory nasal sinuses, etc., should be sought, and when found removed, if possible. If the disease is associated with marked anemia iron and arsenic are indicated. If there is evidence of syphilis arsphenamin, mercury and iodids should be tried. If a malarial element is present quinin may effect a cure. All influences that tend to induce morbid irritability of the nervous system, such as mental or physical fatigue, undue emotional excitement, sexual

*For details see article by Strauss, Jour. Amer. Med. Assoc., Dec. 15, 1917.

excesses, and over-indulgence in tea, coffee, alcohol and tobacco, should be eliminated if possible. An effort should be made also to improve the general nutrition, which in many cases is much impaired. For this purpose an abundance of fresh air, appropriate food, regular hours, adequate protection from vicissitudes of weather, systematic exercise, frequent bathing with friction of the skin, and tonic remedies are requisite. Neuralgia in neurasthenic patients is sometimes successfully managed by the Weir Mitchell treatment or a modified form of it. A change of residence to a warm dry climate is often helpful.

Many special remedies have been recommended but few are worthy of confidence. Dana and others speak favorably of strychnin in heroic doses in *tic douloureux* occurring in anemic and exhausted patients and when the duration of the disease does not exceed one or two years. The drug is given hypodermically once a day and the dose is gradually increased from $\frac{1}{30}$ grain (0.002 gm.) to $\frac{1}{5}$ grain (0.013 gm.), 10 to 12 days being required to reach this maximum. During the treatment the patient should be kept in bed and closely observed.

For the attack itself the coal-tar analgesics (acetphenetidin, antipyrin and acetanilid) are the most generally useful remedies. From 5 to 8 grains (0.3–0.5 gm.) may be given every two to four hours, according to the intensity of the pain. It must be borne in mind, however, that these agents when used repeatedly not only lose their potency but also unfavorably affect the patient's general nutrition. Injections of morphin are undoubtedly the most certain means at our command of affording temporary relief, but on account of the great danger of inducing a habit, this measure should be employed only as a last resort. Combinations of a bromid or of caffein with acetphenetidin or antipyrin are sometimes more effective than the coal-tar analgesics alone. Aconitin ($\frac{1}{400}$ gr.—0.00016 gm.), tincture of gelsemium (10–15 min.—0.6–1.0 mil.), and butyl-chloral hydrate (5–10 gr.—0.3–0.6 gm.) are occasionally serviceable. Neuralgic attacks that are excited by exposure to cold are often favorably influenced by salicylates in large doses.

Local Treatment.—Heat, dry or moist, may be applied for its soothing effect. Occasionally cold applications are more agreeable. Menthol or choral-camphor is useful in mild attacks. A spray of ethyl chlorid is sometimes efficacious, especially in post-zoster neuralgias. In using it about the face, however, the eyes must be carefully protected. Electricity in the form of a mild continuous galvanic current has its advocates. In refractory cases of trigeminal neuralgia the application of a blister back of the ear is sometimes of benefit.

In the majority of cases the attacks eventually become so severe and the remissions so short that recourse must be had to operative treatment, especially alcoholic injection, peripheral neurectomy or avulsion of the sensory root of the Gasserian ganglion. Treatment of trigeminal neuralgia by injection of alcohol (80–95 per cent.) into the nerves near their foramina of exit from the skull, which was introduced by Schlösser in 1903, may be recommended when the pain is limited to one of the two lower divisions of the nerve and even when all three divisions are affected if the patient's condition is such as to unfit him for the more radical Gasserian operation. Moreover, as Cushing has pointed out, it is sometimes useful in determining in doubtful cases whether the syndrome is a true neuralgia of the *tic douloureux* type or one of the peculiar and rare pseudoneuralgias not amenable to relief either by injections or neurectomies. Alcohol injection does not result in a permanent cure, but it usually gives complete relief for an average period of from eight months to a year. It has almost entirely superseded peripheral neurectomy, except in the case of supraorbital neuralgias in which it has not been very effective. Post-zoster neuralgia should not be treated by alcohol injection or by any other operative measure. The injection treatment is safe when properly practiced, but in the hands of the inexperienced it is not uncommonly followed by secondary hemorrhage, oculomotor palsy, facial paralysis, stiff jaw, secondary keratitis or labyrinthine vertigo. The injection of alcohol directly into the ganglion itself has been done with some success, but it seems more likely to result in complications than the radical operation of removing the sensory root. The radical operation almost always affords permanent relief from the pain, although it results in localized anesthesia. In skillful hands the risk is small. Cushing reports 332 operations with 2 deaths in the first 34 and none in the last 298, and Frazier reports a series of 157 consecutive operations with 1 death (0.6 per cent.).

HERPES ZOSTER

(Shingles)

Locally, a dusting powder of zinc oxid (8 parts) boric acid (8 parts) talc (8 parts) and camphor (1 part), or zinc ointment containing 5 grains (0.3 gm.) of menthol to the ounce (30.0 gm.) may be used and the parts covered with a layer of cotton. In outbreaks near the eye, the conjunctiva should be frequently washed with a solution of boric acid. For the relief of pain acetphenetidin, salicylates, bromids and codein may be given. The following combination is often useful:

R. Codeinæ sulphatis..... gr. iss-ii (0.1-0.13 gm.)
 Acetphenetidini
 Acidi acetylsalicylici..... āā gr. xl (2.65 gm.).—M.
 Ft. chartulæ No. xii.
 Sig.—One every three hours.

For protracted cases zinc phosphid, quinin and strychnin and a mild galvanic current have been recommended. Schamberg has obtained rapid amelioration of the pain from the use of the x-ray.

CEREBRAL HEMORRHAGE; CEREBRAL THROMBOSIS AND EMBOLISM

(Cerebral Apoplexy)

Persons predisposed to *cerebral hemorrhage* should be advised to lead a life as free as possible from mental excitement and strenuous physical exercise, to abstain from alcohol, to reduce the intake of food, and, as an additional means of keeping down the bloodpressure, to secure each day a free evacuation of the bowels, using for the purpose, if necessary, some suitable aperient.

The Attack.—Every effort should be made to keep the patient absolutely quiet. If he must be moved, the transportation should be done with extreme gentleness, and the distance reduced to a minimum. The head and chest should be slightly raised. In some cases it may be necessary to draw the jaw and tongue forward to prevent mechanical asphyxia. An ice-bag to the head is useful. A brisk cathartic, such as croton oil (1-2 drops in a little olive oil), may be placed on the back of the tongue to secure prompt catharsis. If the face is congested and the pulse full and strong, venesection to the extent of 8, 10 or 12 ounces is apparently indicated, although Cushing gives experimental evidence to show that the persistent high arterial tension is only an indication of nature's effort to ward off fatal anemia of the bulbar centers brought about by the extreme degree of intracranial tension and that when the blood pressure steadily rises to 250 mm. or higher trepanation is the only measure that holds out any prospect of success. Even if the clot is not found and removed, the relief of the cerebral compression afforded by the operation, it is claimed, may suffice to revive the exhausted bulbar centers, and arrest the alarming symptoms. Important as these observations appear to be, it is doubtful whether they will convince many of the advisability of surgical intervention in any case of cerebral hemorrhage that is not clearly cortical or subcortical.

If the heart action is feeble and the face is blanched diffusible stimulants may be given cautiously, although it is unlikely that

they will prove of much value. Thorough cleanliness, bathing with alcohol, frequent change of position, and the avoidance of roughnesses in the bed are necessary in order to prevent the development of bed-sores. Since blisters are produced more readily than in health, especial care should be taken in using hot applications of any kind. Retention of urine is likely to occur, and if it does the patient must be catheterized.

Even in the mildest cases the patient should not be allowed to leave his bed for two or three weeks, and during this time the diet should be light and unstimulating. The ice-cap should still be kept upon the head. Aconite is often useful in subduing the fever of reaction and in decreasing arterial tension. For restlessness and wakefulness, small doses of a bromid or of chloral may be given.

Chronic Stage.—After the acute symptoms have entirely disappeared, which will rarely be earlier than ten days or two weeks after the attack, massage should be systematically practised. It often contributes to the restoration of power, or when this is impossible, to the prevention of contractures. After the lapse of three or four weeks, triweekly applications of the faradic current may be of service.

In some cases warm saline baths (90°–95° F.) combined with passive movements prove useful adjuvants to massage. Potassium iodid is often prescribed with the hope that it may aid absorbing the clot, but it is of doubtful utility, and, moreover, it is very prone to disturb the digestion.

When symptoms are present in a case of cerebral apoplexy that make the *occlusion of an artery* more probable than extravasation of blood, the treatment should consist in absolute rest, in the use of mild circulatory sedatives or stimulants according to the condition of the pulse, and, if there is much restlessness, the administration of bromids. Venesection is contraindicated. The management of the patient after the attack is that of the chronic stage of cerebral hemorrhage.

TUMOR OF THE BRAIN

If there is the slightest doubt as to the nature of the growth vigorous antisyphilitic treatment should be instituted. In this connection it is well to remember three facts: First, that gummata do not always yield to arsphenamin, mercury and iodids; second, that improvement under these remedies is not positive proof of the gummatous nature of the lesion, because a temporary amelioration of symptoms may also occur in other tumors, notably in gliomata, under antisyphilitic treatment; and third,

that a syphilitic person may have a non-syphilitic tumor. In the absence of urgent symptoms, the antisyphilitic treatment should be continued for several weeks, then if no decided improvement is observed and the tumor is in accessible region (near the surface of the cerebrum, in a lateral lobe of the cerebellum, at the side of the cerebellum and pons, in the neighborhood of the hypophysis), and is clearly not metastatic, operation is indicated as *extirpatory measure*, for the risks of operation in competent hands are much less serious than those of delay. The more strongly the evidence supports the belief that the tumor is single, circumscribed and benign the greater are the probabilities that a cure will result. In the hands of those having the requisite skill the operative mortality may be less than 10 per cent. In a series of 136 cases reported by Cushing the operative mortality was 7.3 per cent., complete recovery occurred in about 5 per cent., recovery with some persistence of symptoms in 10 per cent., and alleviation of symptoms and prolongation of life in 50 to 60 per cent. In series of 112 cases (197 operations) reported by Magnus the operative mortality was 8.2 per cent., clinical cure occurred in 10 per cent., and improvement in 50 per cent. As regards the nature of the tumor, endotheliomata are most often operable and gliomata and metastatic growths are least often operable.

Even when extirpation of the tumor is not feasible craniectomy (*decompression*) over a "silent" area and in a region where adequate muscular support can be given to the bulging brain (right subtemporal and suboccipital regions) is often advisable with the view of saving sight, relieving distress and prolonging life. *Radium* or *x-ray therapy* combined with craniectomy has occasionally given good results, especially in pituitary lesions.

Lumbar puncture is also of some value as a decompressive measure, but it must be employed with great caution, for sudden death may follow the removal of a large amount of fluid, the increased intracranial tension causing the medulla to be forced against the foramen magnum when the intraspinal pressure is relieved.

Except in syphilitic growths, the *medical treatment* of brain tumor is merely palliative. Headache may be relieved to some extent by the administration of coal-tar analgesics in large doses, by the application of ice-bags to the head, and, at times, by the application of dry or wet cups to the back of the neck. The administration of ergot has also been recommended. Eventually, morphin must be given, although it, too, may fail unless the dose is large enough to cause stupefaction. Vertigo and vomiting are sometimes benefited by the administration of bromids or of scopolamin.

INFANTILE CEREBRAL PARALYSIS

Craniotomy and removal of the clot should be considered in cases developing at birth and presenting signs of increased intracranial pressure. Two of four operations performed by Cushing in 1905 yielded good results, and since that date craniotomy has been done by others with more or less success. Lumbar puncture has also proved useful in some cases. In later cases when there is a history of difficult labor and papilledema and increased pressure of cerebrospinal fluid are present the removal of meningeal cysts offers some hope of relief. Sharpe and Farrel report that of 65 cases so treated, 9 of the patients died after operation, 8 within two years, 19 were unimproved, 4 disappeared from observation, and 25 were much benefited. In any case after the acute symptoms have subsided warm baths, massage and passive movements are indicated to counteract the tendency to contractures. If the latter have already appeared relief may be afforded by orthopedic appliances, tenotomies, or, in selected cases, division of several posterior nerve-roots. When the intelligence is impaired training in a special institution offers the best chance of improving it.

CHRONIC HYDROCEPHALUS

This is still unsatisfactory. If there is evidence of syphilis mercury and iodid may occasionally lead to a cure. Ventricular puncture followed by injection of antimeningitic serum has been successful in some cases of hydrocephalus resulting from cerebrospinal fever. In cases of communicating hydrocephalus dependent upon hypersecretion, thyroid extract is worthy of trial, as this drug lessens the secretory activity of the choroid plexus (Frazier and Peet). When the outlets of the ventricles are unoccluded spinal puncture, frequently repeated, may be of benefit, transitory or lasting, according to the nature of the pathologic process. On the other hand, lumbar puncture will not afford even temporary relief if communication between the ventricles and subarachnoid space is obstructed. In this case repeated tappings through the fontanelles may be tried, but it is not likely to prove successful; moreover, the operation is sometimes followed by an inflammatory reaction and an exacerbation of symptoms. Apparently, the most effective method of dealing with obstructive hydrocephalus is puncture of the corpus callosum, this operation providing an outlet for pent-up fluid into the subarachnoid space, where it may be absorbed.

TABES DORSALIS

(Locomotor Ataxia)

General Measures.—Rest, both physical and mental, is of vital importance. Erb advises that the patient should live as if he were an old man, quietly, regularly, and with no excitements. In some cases it is advisable to begin the treatment with complete rest in bed for a week or two. The diet should be non-stimulating and easily digestible. Alcohol and tobacco should be used sparingly, if at all. Sexual excess is exceedingly injurious. Every precaution should be taken to avoid exposure to cold and wet, and, if feasible, the patient should spend the winter months in a warm equable climate. Tepid baths of 80°–85° F. are sometimes of service, but very hot baths and cold baths are usually harmful. Many natural springs have been recommended, the most popular being the Hot Springs of Arkansas, those of Virginia, and those of Los Vegas, New Mexico, in this country, and the thermal baths at Rehme, Nauheim, and Aix-la-Chapelle in Europe. Patients in whom the disease is far advanced, should, of course, be spared the expense and discomforts attendant upon a long journey.

The systematic practice of coördinated movements, as originally recommended by Frenkel (see p. 529), is often successful in lessening the ataxia, the improvement sometimes lasting for years. Even in advanced cases this method of treatment is worthy of trial. If good results are to be secured, however, it must be conducted by a skillful attendant and regularly supervised by the physician himself. If left to the patient it is more likely to prove harmful than beneficial. The exercises are contraindicated when the pains are of frequent occurrence, when there is advanced arterial disease, when there are severe arthropathies, and when there is a tendency to spontaneous fractures. For the details of the "reëducation method" the reader is referred to Frenkel's monograph on the treatment of ataxia. Massage is sometimes of value in that it affords a means of securing some of the benefits of exercise without the expenditure of energy.

Drugs.—In recent cases antisiphilitic remedies should be given a thorough trial, more especially because of the difficulty in determining with certainty whether a case is one of true tabes or of exudative interstitial syphilis of the cord. Even in true tabes, however, some improvement may occur. Courses of arsenic, in the form of arsphenamin, should be given, preferably by the method of Swift and Ellis. According to this method the patient is given intravenously about once a week or once in two

weeks 0.3–0.6 gm. of arsphenamin, and after 30 to 60 minutes is bled to the extent of 50 mils of blood. The serum is then separated from the blood and inactivated at a temperature of 132.8° F. (56° C.) for 30 minutes, and within 24 hours a dose of 20 to 25 mils of undiluted serum or 30 mils of 50 per cent. serum with normal salt solution is introduced by gravity into the spinal canal after an equal amount of cerebrospinal fluid has been removed. The patient should remain in bed 24 or 48 hours after the treatment. In addition to arsphenamin, mercury should be administered by inunction or by hypodermic injection, and an iodid by the mouth. In some cases tonics are also indicated.

Treatment of Special Symptoms.—When the pains are severe the most potent remedial measure is absolute rest in bed. Light touches of the actual cautery or sinapisms over the root of the nerve supplying the affected part occasionally afford relief. Deep massage is sometimes of service. Mitchell has found the alternate application of ice and hot water useful. Flannel bandages applied firmly from the toes up to the middle third of the thigh sometimes do good. A snugly fitting abdominal binder may also be used to lessen girdle pain. Electricity in the form of the faradic brush, static spark, or stabile galvanic anode is worthy of a trial.

The most generally useful anodynes are acetphenetidin, antipyrin and the salicylic compounds. According to Osler, the prolonged use of nitroglycerin, given in increasing doses until the physiologic effect is produced, is of great service in allaying pains and diminishing the frequency of crises in all cases of tabes in which there is increased arterial tension. In some cases drainage of the spinal canal is effective. Eventually, recourse must be had to morphin, but its use should be deferred as long as possible.

Gastric crises may require withholding of food by the mouth for a time, the patient being sustained by nutritive enemas. Lavage is often beneficial. The application of sinapisms over the epigastrium may do good. Morphin hypodermically is sometimes necessary. In refractory cases resection of the posterior roots of the seventh to the tenth dorsal nerves may produce satisfactory results. Numbness and paresthesia sometimes yield for a time to local applications of faradism given with the wire brush. Vesical weakness should receive the most careful attention. The bladder must be thoroughly emptied, if need be by catheterization. On the first appearance of cystitis the bladder should be thoroughly washed out with weak antiseptic solutions.

PARETIC DEMENTIA

(General Paralysis of the Insane)

Treatment includes the avoidance of all mental and physical excitement and the employment of the general measures recommended in cases of neurasthenia. Owing to the difficulty of distinguishing clearly between coarse cerebral syphilis and paretic dementia and to the fact that in the latter the destructive lesions are frequently accompanied by an actual exudative syphilitic process, vigorous treatment with arsphenamin, preferably according to the method of Swift and Ellis, and with mercury should be instituted. Such sedatives as bromids, scopolamin, paraldehyd and trional may be required from time to time to allay mental excitement. For obvious reasons the treatment is best carried out in a well-ordered asylum or sanatorium.

PRIMARY LATERAL SCLEROSIS; AMYOTROPHIC LATERAL SCLEROSIS; PROGRESSIVE SPINAL MUSCULAR ATROPHY;
CHRONIC PROGRESSIVE BULBAR PALSY; DISSEMINATED (MULTIPLE) CEREBROSPINAL SCLEROSIS

Lateral Sclerosis.—Little is to be expected from medication. Occasionally, however, a case that appears to be one of pure lateral sclerosis is benefited by antiluetic treatment. For the spasticity warm baths and massage are advisable. Division of a number of the posterior lumbar roots may also afford relief and is worthy of trial if the spasms are very severe.

Amyotrophic Lateral Sclerosis.—This is unsatisfactory. Rest, warm baths, and massage should be tried, although nothing more than slight temporary benefit has ever resulted from the use of these measures. If there is clear evidence of syphilis antileuetic treatment is indicated.

Progressive Spinal Muscular Atrophy.—Muscular fatigue has a deleterious influence and should be avoided. Massage and electricity are of little service. Strychnin has been recommended by Gowers but it does not appear to influence the progress of the affection. If there are evidences of syphilis (positive Wassermann reaction, scars on the skin, lymphocytosis of the cerebrospinal fluid, etc.) antiluetic remedies should be given a thorough trial.

Chronic Progressive Bulbar Palsy.—As no treatment is known to check the progress of the disease, it is best to aim at promoting the patient's general health by rest, careful feeding, hydrotherapy, massage, and the administration, if necessary, of tonic remedies. When food can no longer be swallowed, recourse should be had to the feeding tube.

Disseminated (Multiple) Cerebrospinal Sclerosis.—This is wholly palliative. Rest, luke-warm baths, and gentle massage sometimes favorably influence the rigidity. Forced feeding may be necessary. Overexertion, mental excitement, sexual excesses, and the use of alcohol and tobacco are to be avoided. If there is anemia, iron and arsenic are indicated. Improvement has been reported from the use of roentgen rays (Marinesco) and also from intramuscular injections of fibrolysin (Crafts).

ACUTE MYELITIS

If possible the patient should be placed on a water-bed or air-bed. If there is evidence of syphilis antiluetic treatment should be instituted. Every precaution must be taken to prevent the development of bedsores. Frequent change of the patient's position, absolute cleanliness of the parts subjected to pressure, and bathing with alcohol and water will do much toward averting this serious complication. Retention of urine must be met by systematic catheterization under strict aseptic precautions. When there is incontinence a carefully adjusted urinal should be employed. Any tendency to cystitis will demand daily irrigation of the bladder with mild antiseptic solutions. Spastic paresis is best treated by warm baths and passive movements. If the patient improves he should be encouraged to carry out himself simple gymnastic exercises and to attempt stepping and other movements, since by so doing he is likely to cultivate a certain amount of compensatory function in tracts of the cord that have not been destroyed.

The treatment of paraplegia the result of spinal caries consists in absolute rest in the recumbent position, fixation and progressive straightening of the spine, and, if necessary, the performance of Albee's bone-grafting operation or laminectomy.

INFECTIOUS CHOREA

(St. Vitus' Dance, Sydenham's Chorea)

Rest of body and mind is the most important factor in the treatment of the disease. No matter how mild the attack, the child should be taken from school. If the symptoms are at all severe rest in bed in a quiet, well-ventilated room should be insisted upon, the bed being well padded on all sides to prevent the patient from injuring himself. To insure complete repose it is often necessary to exclude the child's playmates and even his own brothers and sisters from the room. The diet should be liberal and nutritious.

Gentle massage is sometimes beneficial, especially in poorly nourished children, but no gymnastic exercises should be allowed until convalescence is firmly established. Prolonged warm baths, the temperature of the water being maintained at about 95° F. (35° C.) are often decidedly helpful. Two such baths may be given during the day. In older children, especially in highly neurotic cases, the wet pack may be used with advantage. A change of air, especially a change to the seashore, is of benefit in mild but refractory cases. On account of the marked tendency to relapse, children who have once suffered from the disease should not be overtaxed at school and should be guarded, as far as possible, from attacks of rheumatism.

The employment of drugs is of secondary importance. Arsenic has been extensively used, but its value is at least doubtful. A child of 5 or 6 years may be given as an initial dose 3 minims (0.2 mil) of Fowler's solution three times a day, and this amount may be gradually increased by a minim a day until 10 minims (0.6 mil), three times a day, are being taken. If puffiness about the eyes, nausea, intestinal colic, or diarrhea occur the administration of the drug should be suspended for several days and then resumed at a dose somewhat less than the child was taking when the untoward symptom appeared. Arsenic should always be given after meals and well diluted. While taking large doses the patient should be kept under close observation, as albuminuria, conjunctivitis, inflammatory diseases of the skin or even neuritis may develop independently of the usual untoward effects. Billings speaks very favorably of the use of arsenic in the form of sodium cacodylate subcutaneously or intravenously (10 grains—0.6 gm.—daily in one dose).

Antipyrin in doses of 15 to 20 grains (1.0–1.3 gm.) a day, at six years of age, has been advocated by a number of writers, but when used so freely this drug may cause cyanosis, anemia, and prostration. Salicylates are of service when rheumatism occurs in association with chorea, otherwise they usually fail. Auto-serum treatment, originally proposed by A. Goodman and consisting in withdrawing blood (50 mls) from the patient, separating the serum, and injecting 15 to 20 mls of this into the spinal canal after removing an equal amount of cerebrospinal fluid, has not proved uniformly successful. In a recent report, however, Brown, Smith and Phillips claim far better results from it than from any other method of treatment. In the 23 cases cited a cure was obtained within 3 weeks in 77 per cent. and improvement in 19 per cent. The average number of injections was three. It is important that all drug therapy be suspended before the treatment is begun.

When the movements are violent and interfere with sleep recourse must be had to sedatives. The best are chloral, bromids, phenobarbital and trional. Morphin is rarely indicated. In addition to special medicaments and sedatives, iron is often required to combat anemia.

In chorea insaniens hyoscin hypodermically, in doses of $\frac{1}{200}$ – $\frac{1}{100}$ of a grain (0.0003–0.0006 gm.) twice daily, sometimes acts well. Inhalations of chloroform may be necessary. Forced feeding is occasionally imperative. Cases of chorea complicating pregnancy call for a diet limited to milk and diluents and a systematic eliminative treatment by cathartics, diuretics and diaphoretics. The induction of abortion or premature labor is rarely necessary.

PARALYSIS AGITANS

Although paralysis agitans is incurable, much can be done to alleviate the symptoms and make the patient more comfortable. A life free from worry and excitement, in a congenial environment, and varied by change of climate in the trying seasons of the year is one which best meets the requirements. While the expenditure of energy should be restricted and an abundance of sleep is always necessary, rest-treatment is contraindicated. Luke warm baths, continued for 10 or 15 minutes, and combined with passive movements and active but gentle exercises, may do much toward relaxing the muscular rigidity and overcoming the physical inertia. Swift reports favorable results from simple muscular movements of the different members successively, performed very slowly at the rate of about one foot to the second, with strong mental concentration upon the movement while it is in progress. Vibration, such as is produced by riding in a railway train, sometimes affords considerable comfort. Massage and electricity, however, are of doubtful values. Tonics, especially arsenic and iron, may often be used with benefit. Strychnin is contraindicated. Among the numerous sedatives extolled for their favorable effect upon the tremor, the best is undoubtedly scopolamin hydrobromid. From $\frac{1}{200}$ to $\frac{1}{100}$ of a grain (0.0003–0.0006 gm.) may be given, preferably hypodermically, two or three times daily and continued, with due regard for disagreeable by-effects, for several weeks, if necessary. When there is much restlessness, potassium bromid or codein, in small doses, will be found a useful adjuvant. In the hands of Berkley, Dercum and others parathyroid extract in doses of $\frac{1}{20}$ to $\frac{1}{10}$ grain (0.003–0.006 gm.), three times daily, seemed to be of temporary benefit.

TETANY

The cause should be sought for and removed, if possible. In infants dietetic and hygienic regulations are of prime importance. When there is evidence of rickets, cod-liver oil and phosphorus are of definite value. In the form associated with gastrectasis, lavage, rectal feeding, and proctoclysis with normal saline solution are sometimes of service. If the condition does not improve gastro-enterostomy should be performed. Wirth has collected 21 cases treated surgically, with a mortality of 15 per cent., as compared with a mortality of 50 to 75 per cent. in the cases treated by medical means. In cases occurring during lactation benefit accrues from weaning the child. In all cases rest in bed, frequent warm bathing, and restriction of the diet to light unstimulating foods are general measures of value. Lumbar puncture has proved efficacious in some instances. Calcium is indicated. It may be prescribed as calcium lactate or glycerophosphate. Parathyroid preparations have been employed with some success, but as a rule they have failed. For the spasms themselves, sedatives, such as bromids, chloral, and scopolamin, may be used.

TIC

The treatment of tic consists in removing any existing peripheral irritation which may have served as an exciting cause, such as errors of refraction or intranasal lesions, and in employing general measures to combat the underlying constitutional inferiority. Graduated gymnastic exercises are especially useful. Children subject to tic require careful training and protection from all influences which tend to excite the emotions. In some cases much benefit is derived from the reëducational exercises introduced by Brissaud. Briefly, these are "a combination of immobilization of movements with movements of immobilization." Certain exercises are intended to teach the patient how to preserve immobility, while the object of others is to replace an unwilling movement by one that is willed. The exercises in general have to be performed in front of a mirror. The excellent monograph of Meige and Feindel* should be consulted in this connection.

EPILEPSY

Hygienic treatment is of the utmost importance. Moderate exercise, both mental and physical, is beneficial. Idleness and

* "Tics and Their Treatment," by Henry Meige and E. Feindel. Translated by S. A. K. Wilson, London, 1907.

seclusion have a baneful effect. Adults should follow, if possible, some light and agreeable pursuit, preferably one which will permit them to spend the greater part of the day in the open air, and which will not add to the risk of physical injury should attacks come on without warning. The establishment of so-called epileptic colonies or farms, where patients can be employed in agricultural pursuits, has proved a great boon to many confirmed epileptics of the bread-winning class. Children in whom the disease is well established are better cared for, as a rule, in special institutions or private sanatoria. Home training to be successful usually requires the services of a capable supervisor. The marriage of epileptics should be discouraged.

The diet should be simple, readily digestible, and, in most cases, mainly vegetable. Overloading of the stomach is a potent factor in precipitating attacks. The principal meal is best taken at midday, and full evening meals should be avoided. The claim made by Toulouse and Richet that it is advantageous to reduce the sodium chlorid taken with food to 1 or 2 grams a day has been confirmed by many observers.

Tea, coffee, alcohol, and tobacco should be used very sparingly, if at all. The patient must be constantly warned against excesses of every kind. The digestive functions should be brought to the highest possible state of efficiency. The bowels must be regulated by diet, and, if necessary, by mild aperients. Liberal water-drinking, frequent bathing, followed by friction of the skin, light exercise in the open air, and other measures which favor elimination are to be recommended. General tonics, such as iron, arsenic, and cod-liver oil, are sometimes required to combat anemia and malnutrition.

Although very few cases of epilepsy are purely reflex, peripheral irritation—phimosis, adherent prepuce, worms, a foreign body in the nose or ear, and painful cicatrices—should be carefully sought for, and if found removed.

The most reliable drugs are the bromids, the amount required varies with the severity of the case and the susceptibility of the individual, and must be determined experimentally in each case. A daily dose of from 1 to $1\frac{1}{2}$ drams (4.0–6.0 gm.) of sodium or potassium bromid should not be exceeded. The addition of one or two drops of Fowler's solution with each dose of bromid is useful in preventing the occurrence of acne. When the attacks occur at regular intervals it is advisable to administer the drug in relation to the time of the attacks. Thus, in nocturnal epilepsy a single large dose at bedtime may suffice. Again, in women, when the seizures occur only at the menstrual periods, active medication may be restricted to the week preceding each period.

When the convulsions occur at long intervals and show no tendency to increase in frequency, it is better to dispense with special medication entirely and to rely upon hygienic and dietetic measures to lessen the excitability of the nerve-centers. In every case it is of the utmost importance to limit the dose of the bromids to the smallest possible amount that will control the seizures. Relief that comes only with saturation is dearly purchased.

Luminal, which is barbitol with an ethyl group replaced by one of phenyl, is sometimes a very good substitute for the bromids. In doses of from $\frac{1}{2}$ to 1 grain (0.03–0.065 gm.), two or three times a day, it can often be taken for long periods without untoward effects. Psychic depression and apathy, however, may occur, and occasionally the drug seems actually to increase the tendency to seizures. In nocturnal epilepsy chlorbutanol (chloretone), in doses of 5 grains (0.3 gm.) is sometimes a useful adjuvant to the bromids. Horse-nettle is another remedy that may increase the efficacy of the bromids. From $\frac{1}{2}$ to 1 dram (2.0–4.0 mls) of the fluidextract may be given thrice daily. Turner speaks favorably of Glineau's dragées (six a day), which contain potassium bromid, 1 gram; picrotoxin, $\frac{1}{3}$ mg.; and antimony arsenate, $\frac{1}{2}$ mg. Dercum and Mills have found small doses of thyroid extract useful in some cases. When the circulation is weak a combination of digitalis with the bromids sometimes proves efficacious.

Surgical Treatment.—Trephining offers some hope of relief in certain cases of epilepsy, although it has to its credit less than 4 per cent. of recoveries. It is definitely indicated in traumatic cases if there is evidence of cranial injury and the traumatism stands in direct causal relation to the attacks. It is also indicated in Jacksonian epilepsy if there is any evidence other than the fits of a coarse cortical lesion. According to Matthiae, of 326 cases of traumatic epilepsy (60 of the general and 266 of the Jacksonian type) treated surgically, cure or recovery lasting several years occurred in 96, of which 81 were of the Jacksonian type.

Treatment of the Attack.—When an aura is perceived it is often possible to arrest the paroxysm by the inhalation of amyl nitrite. Patients may provide themselves with this drug in the form of "pearls" which may be crushed in the handkerchief. When the attack is preceded by a local spasm forcible extension of the part sometimes succeeds in aborting it. If a sensory aura is felt in a limb the part may be firmly grasped or encircled with a tight ligature. The patient himself often learns by experience some method by which he can suppress seizures of which there is due warning. During the attack there is little to be done beyond protecting the patient from injuring himself. If necessary, inhala-

tions of amyl nitrite or of chloroform may be used. In the status epilepticus the most reliable measures are inhalations of chloroform, hypodermic injections of scopolamin ($\frac{1}{100}$ gr.—0.00065 gm.) or of morphin ($\frac{1}{4}$ gr.—0.016 gm.), enemata of chloral (20–30 gr.—1.3–2.0 gm.) and hot baths.

NEURASTHENIA

The treatment of neurasthenia must vary with the cause of the disease and the circumstances and idiosyncrasies of the patient. In every case an earnest effort should be made to determine the exciting cause and to remove it if possible. With this in mind, the family history of the patient, his occupation, habits, and amusements, and the condition of his various organs must be carefully studied.

In the milder forms of the disease, especially when overwork has been the exciting factor, a month or two of rest with change of scene will often effect a cure. In such cases quiet travel, so planned that it will interest the patient without fatiguing him, is frequently attended with excellent results. A prolonged sea-voyage is sometimes very useful. In other cases the “wilderness cure” of S. Weir Mitchell may be recommended with advantage.

In the absence of any special gastric disturbance, the diet should be simple, readily digestible, and abundant. Tea, coffee, alcohol, and tobacco are better avoided. A tepid sponge bath in the morning, provided it be followed by a good reaction, is beneficial. The wet pack, sitz-bath, spinal douche, and Scottish douche are of service in individual cases.

When the fatigue symptoms are marked, *rest* is imperative. This may be relative or absolute. In some cases the addition of from three to five hours to the time usually spent in bed, or a rest in bed of a few hours during the day will suffice. When, however, the symptoms are severe it will be necessary for the patient to give up all work for a period of from 4 to 8 weeks. In such cases good accrues from the “rest cure” introduced by S. Weir Mitchell. This treatment includes not only rest but also isolation, a liberal diet of easily digested foods, and artificial muscular exercise. The details must vary, of course, in each case, and only the outlines can be given here. The full rest treatment is especially applicable to neurasthenic women; indeed men, unless they are extremely prostrated, cannot often tolerate it.

Rest.—For the first two or three weeks at least rest must be absolute, the patient not being allowed to feed himself nor to leave the bed to pass urine or to empty the bowels. As to this point Mitchell says: “In some instances I have not permitted the

patient to turn over in bed without aid, and this I have done because sometimes I think no motion desirable and because sometimes the moral influence of repose is of use." As improvement becomes manifest some relaxation is permissible, and the patient may be allowed to sit up in bed to take meals and to indulge for a short time each day in reading or simple games. After four or five weeks he may be permitted to sit up in a chair for five or ten minutes a day, the time being gradually lengthened, while at the end of a week or ten days he is up for from three to four hours. Active exercise is now cautiously introduced, and soon he is allowed to go out for a short walk or a drive. Finally, it is desirable that he should spend a week or two at the seashore or in the country before returning to his home.

Isolation.—This is an essential element in the treatment. No one should be permitted to see the patient except the medical attendant and the nurse. Even the writing and receiving of letters are to be forbidden. The permanent return of the patient at the close of the treatment to his family and friends should be effected very gradually. Any infringement of these rules is almost sure to mar the success of the treatment.

Feeding.—In most cases the diet at first should be restricted to milk. From 4 to 5 ounces should be given every two hours, and this amount gradually increased until at the end of a week or ten days from 8 to 10 ounces are given every two hours. Little by little solid food may now be added until at the end of two or three weeks the patient is getting each day three full meals with from 3 to 4 pints of milk in the intervals. The solid food may include stale bread with butter, soft-boiled or poached eggs, thoroughly cooked cereals, oysters, sweet-breads, boiled or roasted meats, green vegetables, cooked fruits, milk-puddings, and ice cream. The evening meal should be light.

Artificial Exercise.—This is supplied in the form of massage and electricity. Through these measures the good effects of active exercise can be secured in a measure without the expenditure of any energy on the part of the patient. Massage should not be practised until the second or third day of the treatment, and even then it should be introduced very gradually. At first the séances should not last longer than a few minutes, but ultimately they may be increased to an hour a day. It is very important, as Dercum has urged, that the massage be performed by the nurse instead of another person with whom the patient would have to become acquainted.

Electricity is the least necessary part of the treatment. It is, however, a useful adjuvant. Like the massage it should be introduced very gradually, otherwise it is likely to excite the patient

and so prove harmful. A slowly interrupted faradic current is generally preferred. This should be applied once a day to each group of muscles in such strength as to elicit slight contractions.

Success in the rest treatment will depend quite as much upon the way in which the various measures are applied as upon the measures themselves. The fact must not be lost sight of that suggestion and discipline play a conspicuous part in the treatment; hence the importance of having all the details systematically and strictly carried out. It is always advisable to furnish a program indicating exactly what shall be done at each hour of the day. It is absolutely necessary that the nurse chosen to conduct the treatment shall be not only skillful and robust but also discrete, tactful, and agreeable to the patient. Finally, the more thoroughly the physician is able to inspire confidence in the patient and to convince him that his disease is not an incurable one, the more likely is he to effect a cure.

Drugs are of little value except in meeting underlying conditions and in combating special symptoms. When there is anemia, iron and arsenic will be found useful. Small doses of strychnin are sometimes beneficial, but more often the drug is useless or actually harmful. Indigestion may be sufficiently severe to demand a modification of the dietetic treatment and the use of special remedies. Such drugs as *asafetida*, *valerian*, and *sumbul* are sometimes helpful.

Every effort should be made to secure sleep by general measures—tepid baths, wet-packs, and gentle massage—before resorting to drugs. If a somnifacient becomes absolutely necessary, a bromid, barbitol, or chloralamid or trional may be given. Chloral and morphin should be withheld on account of the grave danger of inducing a drug habit. Severe headache may call for an occasional dose of acetphenetidin or of a bromid. Constipation can usually be controlled by diet and abdominal massage, but in some cases mild laxatives, such as *cascara sagrada*, sodium phosphate, or the combination of aloin, belladonna, and strychnin, will be required.

HYSTERIA

By proper mental, moral, and physical training much can be done to prevent the occurrence of hysteria in those who through inheritance are predisposed to the disease. Prophylactic treatment includes the inculcation of absolute obedience, self-restraint, and self-denial, a judicious education, suitable outdoor exercise, hygienic surroundings, temperate living, and the avoidance of all that tends to morbid emotionalism or sentimentalism.

In developed hysteria treatment must be directed both to the mind and the body, but especially to the former. To be successful the physician must be able to inspire absolute confidence and faith in the mind of the patient. She must be impressed repeatedly with the fact that her condition is a curable one, and that with her thorough coöperation restoration to health will certainly follow. To intimate that her symptoms are feigned or are wholly within her control is an egregious error. The physician's authority must be unquestioned and his instructions must be rigidly carried out. Want of firmness and of decision is a common cause of failure. Harsh measures are occasionally needed, but they should be adopted only after the most careful consideration. In many cases no method of treatment proves successful until the patient has been removed from her customary surroundings and separated from her sympathetic relatives and friends.

Suggestion is employed consciously or unconsciously in the treatment of hysteria by every successful physician. Without it most of the remedies recognized as efficacious become wholly impotent. The cures which are said to have resulted from the application of magnets and of various metals (metallotherapy) to the surface of the body are now known to have been due solely to suggestion. Complete hypnotism is by no means so generally useful as continuous suggestion. Certain symptoms—paralysis, aphasia, blindness, anesthesia—are sometimes removed by a single hypnotic séance, but on the whole the action of hypnotism is disappointing. Moreover, in the event of failure, it is likely to lower still further the will-power and to increase the emotional instability.

According to Freud, hysterical manifestations cannot be successfully combated in many cases unless the patient's defensive inhibitions are removed by admitting to consciousness his suppressed reminiscences through a process of verbal reaction, and to accomplish this one must have recourse to psycho-analysis, which consists in a careful examination of each neurotic's sexual life history, even that of his early childhood, or as Putnam expresses it, in an inexorable scrutiny of the unconscious regions of his memories and thoughts, with particular reference to his sexual life. Much importance is attached also to dream analysis, for it is held by Freud and his followers that dreams are symbolic and reveal to those skilled in their interpretation the sexual aberrations and unsatisfied desires which in his waking moments the patient unconsciously suppresses. Doubtless, psycho-analysis has sometimes proved of service in hysteria, probably in ways other than those suggested by its author, but its practice

had better be left to the trained psychologist, as in the hands of the unskillful it is certainly likely to do more harm than good.

The physical conditions of the hysterical patient must not be neglected. In mild cases general measures, such as change of scene, graduated exercise in the open air, hydrotherapy, and massage, usually suffice. In severe forms of the disease the treatment that is associated with the name S. Weir Mitchell (see p. 722) often yields excellent results, but it is not always appropriate, and considerable judgment must be exercised in the selection of suitable subjects for it.

Apart from their psychic effect drugs have little influence on hysteria. They must often be used, however, to meet underlying conditions and to combat special symptoms. Iron and arsenic are useful when there is anemia. Antispasmodics, such as valerian, asafetida, sumbul, and camphor, are sometimes helpful, probably in consequence of their impressive odor and taste. Occasionally, direct sedatives, such as the bromids, chloralamid, barbital, or acetphenetidin, may be required, but the continuous use of such remedies is always to be condemned. Powerful narcotics, such as morphin, chloral, and alcohol, are decidedly dangerous.

When hysteria is complicated by local disease special treatment may be necessary, but no surgical operation should ever be performed merely in the hope of relieving hysterical symptoms.

Special Symptoms. *Convulsions.*—Isolation of the patient is imperative. Firm pressure over an hysterogenic zone, particularly one of the ovaries, is sometimes successful. The effusion of cold water on the face may be useful. Inhalations of amyl nitrite or even of chloroform may be employed, if necessary. Emesis induced by apomorphin has yielded good results in some instances. *Hyperesthesia* and *pain* often yield to electricity, light massage and cold douching. In the case of *paralysis* the patient should be instructed how to regain by long-continued practise the use of the affected part. This process of reëducation demands the exercise of great patience and firmness. Swedish movements, massage and faradization are useful adjuvants. *Aphonia* is often successfully treated by the faradic current, one electrode being placed over the larynx and the other over some indifferent point.

Contractures are best treated by passive movements, electricity and suggestion. In refractory cases with secondary changes in the tendons and fibrous tissues it may be advisable to straighten the limb forcibly under anesthesia.

WRITERS' CRAMP

Whatever the plan of treatment adapted the results are likely to prove more or less disappointing unless the patient refrains from writing for at least one or two years. Even under the most favorable conditions work can only be resumed slowly and gradually. Education of the left hand is desirable, although that member also is likely to become affected in time.

Writing is sometimes facilitated by using a light splint which has been shaped to the forearm and wrist and to which is attached a wooden ball fitted to the palm of the hand and carrying a penholder, or by thrusting the penholder through a large rounded cork that can be grasped by the palm and base of the thumb. The object of such contrivances is to substitute movements of the entire arm and shoulder for those of the fingers and wrist. A change of occupation, however, is the best treatment. The general therapeutic measures suggested for neurasthenia are usually indicated. Massage, hot and cold douches, and electricity (mainly for its psychic effect) may be beneficial. In some instances Bier's treatment—the application of an elastic bandage above the elbow for half an hour twice a day—appears to have been of service.

MIGRAINE

In the interval between the attacks it is necessary to make careful search for the various forms of peripheral irritation that are known to have an unfavorable influence on the nervous system, such as gastrointestinal disturbances, eye strain, etc., and to remove, if possible, any of these that may be found. Especially important it is to limit the diet to simple easily digested food, and to exclude all articles that the patient has found by experience to disagree. Alcohol and tobacco are, as a rule, better avoided. An abundance of fresh air, daily sponge bathing, gentle exercise in the open air, and a quiet life are indicated. Constipation must be relieved by dietetic and hygienic regulations, or, if necessary, by the use of saline or vegetable laxatives. The following draft suggested by Starr sometimes acts very well:

R.	Sodii phosphatis exsiccati.....	℥iv (15.0 gm.)
	Sodii sulphatis exsiccati.....	℥x (40.0 gm.)
	Sodii salicylatis.....	℥ii (8.0 gm.)

M.—Triturate and cork tightly.

Sig.—One teaspoonful in a large tumbler of hot or cold seltzer water daily on rising.

A mercurial aperient, once or twice a month, may often be prescribed with advantage. When there is pronounced intestinal stasis, thorough irrigation of the large intestine once a week with plain water is sometimes helpful.

Medication between the attacks is not often effective. Oppenheim reports good results from the prolonged use of arsenic. Thyroid extract in small doses is occasionally of service. When the attacks are especially frequent a combination of sodium salicylate (10 gr.—0.6 gm.) with sodium bromid (15 gr.—1.0 gm.), thrice daily, may afford considerable relief. If taken at the earliest premonition, nitroglycerin ($\frac{1}{100}$ gr.—0.00065 gm.), a large dose of bromid, a full dose of caffein or a cup of strong coffee will sometimes abort an attack. Less frequently a single large dose of sodium salicylate (20–30 gr.—1.3–2.0 gm.) with a brisk cathartic will have a similar effect.

The Attack.—The patient should be kept at rest in a quiet, darkened, well-ventilated room. Hot or cold applications may be made to the head according to individual preference. In some cases a sinapism at the back of the neck and a hot mustard foot-bath mitigate the pain. The application of menthol to the forehead and temples is also soothing. The most useful remedies are acetphenetidin, antipyrin, salicylic acid derivates, bromids, caffein and cannabis indica. The various combinations of these drugs should be tried. Such a combination as the following sometimes affords relief:

R. Caffeinæ citratæ..... gr. xx (1.3 gm.)
 Antipyrinæ..... ʒiiss (6.0 gm.)
 Sodii bromidi..... ʒiiss (10.0 gm.).—M.
 Fiant chartulæ No. xii.
 Sig.—One in water every two hours, if needed.

Cannabis indica is sometimes very useful, when a reliable preparation can be secured. Two drops of the fluidextract may be given every half hour until the pain abates or until slight dizziness or mental confusion appears. Even larger doses may be used, if necessary. Morphin should never be employed except as a last resort.

RAYNAUD'S DISEASE

It is requisite to avoid all influences likely to excite an attack. When cold is the chief excitant, residence in a warm climate during the winter months usually affords great relief. A regimen tending to increase the patient's vasomotor stability and resistance is also of prime importance; thus, an abundance of

fresh air, of sleep, and of nutritious, easily digestible food, warm clothing, lukewarm salt baths, moderate outdoor exercise, and gentle massage are to be recommended. General tonics, such as iron, arsenic, strychnin, and quinin, are frequently indicated, but no medicines have as yet yielded very satisfactory results. Even nitroglycerin, from which much was expected, is of little value as a prophylactic, although in large doses it is sometimes of service in attacks of local syncope or asphyxia. In a few instances calcium lactate in large doses seems to have influenced favorably attacks of local asphyxia. Electricity in the form of the galvanic hand bath or high-frequency currents, if it can be tolerated, may favorably influence the vasomotor symptoms. The application of a tourniquet to the arm or leg, according as the fingers or toes are affected, although extremely painful, may prove decidedly helpful (Cassirer, Cushing, Osler). Venous hyperemia by Bier's method is worthy of trial. Relief is sometimes afforded by moderate dry heat, lukewarm fomentations, or alternate hot and cold douches. Hot drinks are beneficial. For severe pain antipyrin or acetphenetidin may be tried, but morphin will often be demanded. In the treatment of gangrene the usual rules of surgery must be followed.

ANGIONEUROTIC EDEMA

Removal of the cause if it can be discovered is of the first importance. Careful regulation of the diet and the maintenance of free action of the bowels, preferably with salines, sometimes give good results. In the allergic type desensitization through subcutaneous injections of the offending protein may effect a cure. In obscure cases quinin, calcium chlorid, antacids, and especially salicylates are the remedies most worthy of trial. Duhring found sodium hyposulphite, in doses of from 10 to 15 grains (0.6–1.0 gm.) to act well. In a case occurring in a syphilitic, reported by Burr, a dose of arsphenamin effected a permanent cure. Severe gastrointestinal symptoms may require the external application of heat and the administration of morphin and atropin, and edema of the larynx, spraying with a solution of epinephrin (1:10,000) scarification, or even tracheotomy.

ACROPARESTHESIA

Treatment consists in avoiding the deleterious influences likely to cause the disturbance, and in employing measures that tend to increase the patient's resistance. Tonics, hydrotherapy, mas-

sage, electricity (galvanism, static spark, high frequency currents, faradic brush) are sometimes of service. Among special remedies that seem to have been beneficial in individual cases may be mentioned bromids, iodids, ergot, quinin, and thyroid extract.

THERMIC FEVER; HEAT EXHAUSTION; HEAT CRAMPS

In prophylaxis much importance attaches to maintaining the bodily health and vigor by avoiding over fatigue and alcoholic and other excesses. The food should be sufficiently nutritious, but light and unstimulating. The clothing should be light and loose. Cold water should be taken freely. Cool or cold baths should be used frequently.

In **thermic fever** immediate reduction of the patient's temperature is essential. This is best accomplished by a cold bath to which ice is added, but if this is not available cold affusions may be employed or the body may be rubbed with pieces of ice. An ice-cap should be kept on the head. Ice-water enemas may also be administered. Whatever its form, the cooling process should be discontinued when the thermometer in the mouth registers 101° F., as the temperature usually continues to fall after the patient is removed to bed. Antipyretic drugs, such as acetphenetidin and antipyrin, are, as a rule, better avoided, although they may be used cautiously if the means of applying cold are not immediately at hand. The antipyretic treatment must be repeated whenever the high temperature recurs. Venesection (200 to 400 mils) is often of value in the asphyxial form, indicated by lividity, distention of the veins, and signs of pulmonary edema. Weakness of the pulse need not be regarded as a contraindication, as the circulation often improves with the abstraction of blood. Supplementary proctoclysis with normal saline solution may be of service. In some cases lumbar puncture is even more useful than venesection. Marked circulatory depression should be met by the use of stimulants, preferably caffein-sodium benzoate, camphor and strychnin, failure of respiration by artificial respiration, and convulsions by the administration of sedatives (bromids, chloral, morphin). Light nourishment should be given at somewhat frequent intervals and the bowels kept active, by the use, if necessary, of mild salines.

The treatment of **heat exhaustion** consists in the use of external heat, the hypodermic injection of stimulants (caffein, camphor, strychnin, and digitalis), and, in severe cases, hypodermoclysis or proctoclysis with normal saline solution. For the relief of **heat cramps** warm baths and hypodermic injections of morphin are recommended. In the more severe cases, Welsh

has used apomorphin, in doses of $\frac{1}{20}$ to $\frac{1}{12}$ grain (0.003–0.005 gm.), with pronounced success.

COMMON DISEASES OF THE SKIN

ACNE VULGARIS

Unless concomitant systemic disturbances are corrected, local treatment may prove ineffectual. Digestive derangements and constipation are important accessory factors in many cases and call for a careful regulation of the diet and appropriate medication. In anemic, debilitated persons such drugs as iron, nux vomica and cod-liver oil (if well-borne) are often of service. Outdoor exercise, frequent bathing and free-water drinking are valuable aids to recovery. Vaccine treatment, especially the conjoint use of *Staphylococcus albus* (50 to 500 million) and so-called *Bacillus acne* (3 to 5 million), sometimes gives good results in the pustular form of the disease.

Local Treatment.—In acute cases mild applications, such as the following calamin (zinc carbonate) lotion should be used:

- ℞. Pulveris zinci oxidi..... ʒiii (12.0 gm.)
 Pulveris calaminæ..... ʒii (8.0 gm.)
 Glycerini..... fʒi (4.0 mils)
 Liquoris calcis..... fʒvi (180.0 mils).—M.

In chronic cases sebaceous plugs should be removed by frequent washing with mild soap and warm water, by thorough sponging with hot water, or, if necessary, by a special comedo extractor. Applications of a stimulating character are required, the best being those containing mercury, sulphur, or resorcin.

Mercury may be used in the form of a lotion or ointment.

- ℞. Hydrargyri chloridi corrosivi..... gr. ss-ii (0.03–0.13 gm.)
 Tincturæ benzoini compositæ..... fʒi (4.0 mils)
 Emulsi amydalæ amaræ..... fʒiv (120.0 mils).—M.
 ℞. Hydrargyri oxidi flavi..... gr. x-xx (0.6–1.3 gm.)
 Unguenti aquæ rosæ..... ʒi (30.0 gm.).—M.

If there is much pustulation and the lesions are deep-seated an ointment of ammoniated mercury—30 to 40 grains (2.0–2.6 gm.) to the ounce (30.0 gm.)—often acts well.

Sulphur may be used in the form of “lotio alba.”

- ℞. Zinci sulphatis
 Potassii sulphidi..... āā ʒi (4.0 gm.)
 Aquæ rosæ..... fʒiv (120.0 mils).—M.

or Kummerfeld's lotion:

- ℞. Sulphuris præcipitati..... ʒiv (15.0 gm.)
 Pulveris camphoræ..... gr. x (0.6 gm.)
 Pulveris tragacanthi..... gr. xx (1.3 gm.)
 Liquoris calcis
 Aquæ..... āā fʒii (60.0 mils).—M.

or in ointment containing from $\frac{1}{2}$ to 2 drams (2.0–8.0 gm.) of precipitated sulphur to an ounce (30.0 gm.) of lard or cold cream. Resorcin is, as a rule, best prescribed as a lotion containing 5 to 20 grains (0.3–1.3 gm.) of the drug to an ounce (30.0 mls) of water. Boric acid (20 gr.—1.3 gm.) may often be added with advantage.

In refractory cases with deep-seated lesions mild x-ray applications sometimes effect a cure. Repeated applications of the high-frequency current have also been recommended (Stelwagon).

ECZEMA

Internal Treatment.—Constitutional disturbances should always receive careful attention. Tonics are often indicated. In strumous children cod-liver oil, if well borne, may be of considerable value. Derangements of the digestive tract are frequently present and will require a regulation of the diet and appropriate medication. Constipation, especially, must be corrected. Gout, diabetes and chronic nephritis sometimes appear to be in etiologic relationship with eczema, and if this is the case suitable treatment must be directed to these conditions. There are no special remedies of much value. Arsenic is occasionally of service in chronic scaly types of the disease, but it is absolutely contraindicated in all acute or subacute phases characterized by bright redness, burning or itching, or oozing.

External Treatment.—In acute cases with pronounced inflammatory symptoms soothing applications should be employed. A saturated solution of boric acid may be dabbed on for several minutes, allowed to dry, and followed by a dusting-powder of zinc oxid, talc, or magnesium carbonate, or by zinc oxid ointment. The following lotion is also frequently used:

R. Zinci oxidi
Calaminæ..... āā ʒiii (12.0 gm.)
Glycerini..... f ʒss (2.0 mls)
Liquoris calcis..... q. s. ad f ʒviii (250.0 mls).—M.

If there is much itching, $\frac{1}{2}$ to 1 dram (2–4 mls) of phenol may be added to the last lotion.

In all cases of acute eczema soap and water should be used as infrequently as possible.

In subacute eczema salicylic acid, resorcinol, ammoniated mercury or tar may be added to lotions or ointments.

R. Amyli
Zinci oxidi..... āā ʒiii (12.0 gm.)
Acidi borici..... ʒi (4.0 gm.)
Acidi salicylici..... gr. v–x (0.3–0.6 gm.)
Petrolati..... q. s. ad ʒi (30.0 gm.).—M.

In pustular forms of eczema an ointment of ammoniated mercury usually acts well. From 5 to 20 grains (0.3–1.3 gm.) may be added to the ounce (30.0 gm.) of zinc ointment or to the ounce (30.0 gm.) of Lassar's paste:

R.	Hydrargyri ammoniati.....	gr. v-xx (0.3–1.3 gm.)
	Zinci oxidi.....	
	Amyli.....	āā ʒiv (16.0 gm.)
	Petrolati.....	ʒi (30.0 gm.).—M.

In chronic eczema crusts and scales should be removed with petrolatum, olive oil, or, if necessary, with starch poultices. The most useful remedial applications are those containing ammoniated mercury, resorcin, salicylic acid and tar.

R.	Phenolis.....	gr. x (0.6 gm.)
	Hydrargyri ammoniati.....	gr. xx-xl (1.3–2.6 gm.)
	Unguenti zinci oxidi.....	ʒi (30.0 gm.).—M.
R.	Unguenti picis liquidæ.....	ʒi-ʒii (4.0–8.0 gm.)
	Unguenti zinci oxidi.....	q. s. ad ʒi (30.0 gm.).—M.
R.	Resorcinolis.....	gr. x-xxx (0.6–2.0 gm.)
	Acidi salicylici.....	gr. v-x (0.3–0.6 gm.)
	Unguenti aquæ rosæ.....	ʒi (30.0 gm.).—M.

Whatever agent is selected, it is always advisable to use at first a relatively low concentration and to increase the strength cautiously, if the condition requires it, otherwise an irritant rather than a healing effect may be produced.

Finally, in sluggish indurated patches of eczema the roentgen ray sometimes acts very favorably.

PSORIASIS

The general health of the patient sometimes requires attention. Digestive disturbances, constipation, anemia, etc. should receive appropriate treatment. A low protein diet is believed by some observers (Schamberg, Bulkley) to have a favorable influence on the disease. A mild, warm climate, as a rule, acts favorably. Of special remedies, the most generally useful are arsenic, in the form of Fowler's solution by the mouth or of sodium cacodylate hypodermically, potassium iodid in increasing doses, alkalis, and salicylates. No one remedy is uniformly satisfactory and in many cases all of them fail. Arsenic is contraindicated in actively inflammatory phases of the disease.

Local Treatment.—Before active medication is instituted the scales should be removed by warm alkaline baths, followed by friction with soap and water, or an ointment of petrolatum con-

taining 10 grains (0.6 gm.) of salicylic acid (30.0 gm.) to the ounce. The most reliable local remedies are chrysarobin, tar, resorcin, ammoniated mercury, and pyrogallic acid. Chrysarobin is most suitable for cases in which the number of patches is relatively small. As it stains the skin, as well as the clothing, it should be applied only to the patches themselves, and in no case should it be used about the face, as its entrance into the eye results in severe conjunctivitis. The drug may be prescribed in an ointment containing from 10 to 30 grains (0.6–2.0 gm.) to the ounce (30.0 gm.) or in flexible collodion containing about 30 grains (2.0 gm.) to the ounce (30.0 gm.). Salicylic acid—10 grains (0.6 gm.) to the ounce (30.0 gm.)—sometimes increases the efficiency of the ointment.

Tar is a valuable remedy and may be used in the form of the official ointment diluted, with from 6 to 3 parts of petrolatum or lard, or as oil of cade, similarly diluted. Resorcin is sometimes efficacious. It may be used in ointment containing from 20 to 40 grains (1.3–2.6 gm.) to the ounce (30.0 gm.). Ammoniated mercury is especially useful for lesions about the face and scalp. It is not suitable for large patches on the body. It is applied in ointments of about the same strength as those of resorcin, and a combination with the latter or with salicylic acid not rarely acts well. Pyrogallic acid is, on the whole, much less useful than the other remedies and if applied too freely may induce serious or even fatal poisoning through absorption. It is applied in lard or petrolatum in the strength of from 20 to 30 grains (1.3–2.0 gm.) to the ounce (30.0 gm.).

Heliotherapy in the form of sunlight or arc light and roentgen radiation sometimes yield excellent results, and may be used advantageously in conjunction with the prolonged baths (several hours) recommended by Hebra.

RHUS POISONING

(Ivy Poisoning)

Dermatitis caused by contact with poison ivy (*Rhus toxicodendron*), poison sumac, or primrose is best treated by bathing the affected parts thoroughly but gently with warm water and then applying first a solution of sodium thiosulphate, $\frac{1}{2}$ dram (2.0 gm.) to the ounce (30.0 mils) or equal parts of black wash (see p. 395) and lime-water, and finally ordinary zinc ointment. Boric acid, 10 grains (0.6 gm.) to the ounce (30.0 gm.), may be added advantageously to the solution of sodium thiosulphate. A 3 to 5 per cent. solution of potassium permanganate also acts well, but it should not be applied to the face as it stains the skin.

Large vesicles should be opened and drained before the medicated lotion is applied.

Schamberg has produced temporary immunity to ivy poisoning in susceptible persons by administering the tincture of rhus toxicodendron in minute but increasing doses. He prescribes:

- R. Tincture of rhus toxicodendron..... 1.0 mil
 Rectified spirit..... 5.0 mls
 Syrup of orange, sufficient to make 100.0 mls.

The patient is directed to take a drop of the mixture in half a glass of water after meals and to increase the dose by a drop at each succeeding meal until 21 are reached, when a *teaspoonful* is to be taken *once* a day throughout the ivy season. The immunity lasts for about a month. Schamberg has found the same mixture useful also in the treatment of ivy dermatitis.

BOILS

(Furunculosis)

Any underlying constitutional condition which may be etiologically related to the furunculosis should receive careful attention. Regulation of the diet, the administration of tonics and a temporary change of climate may be valuable aids to recovery in refractory cases. The lesions may sometimes be aborted by an application of mercury and ichthyol:

- R. Ichthyolis..... gr. xx (1.3 gm.)
 Extracti belladonnæ..... gr. xxx (2.0 gm.)
 Unguenti hydrargyri..... ʒiss (6.0 gm.).—M.
 Srg.—Apply locally and make pressure with strips of adhesive plaster.

After the occurrence of suppuration free incision and drainage are indicated.

Secondary inoculations may often be prevented by thoroughly cleansing the contiguous parts with warm water and soap and then bathing them with a solution of corrosive sublimate (1:5000). In recurrent furunculosis the most effective measures appear to be the use of vaccines, preferably autogenous, and the administration of brewer's yeast (a teaspoonful to a tablespoonful three times a day) or of compressed yeast ($\frac{1}{2}$ to 1 cake three times a day before or after meals). Calx sulphurata, in doses of from $\frac{1}{10}$ to $\frac{1}{6}$ of a grain (0.006–0.01 gm.), has also been recommended, but it usually fails.

IMPETIGO CONTAGIOSA

This contagious inflammatory disease, which is especially common in children, usually yields readily to frequent and thorough applications of an ointment containing from 10 to 20 grains (0.6–1.3 gm.) of ammoniated mercury to the ounce (30.0 gm.) of cold cream. To prevent autoinoculation, a lotion of mercuric chlorid (1:5000) may be applied, as well as the ointment, both to the lesions and to the surrounding parts.

URTICARIA

(Hives)

The cause should be carefully sought for and removed, if possible. Sensitization to certain articles of food, such as fish, crabs, lobsters, clams, strawberries, etc. is sometimes responsible for the disease. Some disturbance of digestion is the underlying condition in the majority of cases. An association with asthma, jaundice, gout, diabetes, purpura and angioneurotic edema is not rarely observed. In certain chronic cases the etiologic factor remains obscure.

Acute cases usually yield readily to a saline purgative, a light diet, and a salicylate in some form. The following combination often acts favorably:

℞. Acetphenetidini..... gr. xl (2.6 gm.)
 Salophen..... ʒi (4.0 gm.)
 Potassii bitartratis..... ʒiiss (6.0 gm.).—M.
 Fiant chartulæ No. xii.
 SIG.—One every three or four hours.

In refractory chronic cases, without apparent cause, a diet composed for the most part of milk, farinaceous foods, and vegetables, is, as a rule, most suitable. Laxatives, especially magnesia or Epsom salt, are often beneficial. So-called intestinal antiseptics are sometimes of service. Among internal remedies worthy of trial in obscure cases may be mentioned: salicylates, antacids, calcium lactate, quinin (3 gr.—0.2 gm. thrice daily), pilocarpin ($\frac{1}{40}$ gr.—0.0016 gm. thrice daily subcutaneously), atropin, and thyroid extract. Locally, anti-pruritic remedies are almost always required. The following lotion usually suffices:

℞. Phenolis..... ʒiiss–ʒii (6.0–8.0 gm.)
 Acidi boricæ..... ʒi (30.0 gm.)
 Glycerini..... fʒi (4.0 mls)
 Aquæ..... q. s. ad Oi (500.0 mls).—M.

Occasionally, an ointment gives better results. The following is often of value:

R.	Mentholis.....	gr. xx (1.3 gm.)
	Phenolis.....	gr. xxx (2.0 gm.)
	Acidi borici.....	℥iss (6.0 gm.)
	Adipis.....	℥ii (60.0 gm.).—M.

RINGWORM

Ringworm of the Body (*Tinea Circinata*).—Treatment consists in the applications of such parasitocides as sulphur, sodium thiosulphate (sodium hyposulphite), mercuric chlorid.

R.	Sulphuris præcipitati.....	℥i (4.0 gm.)
	Zinci oxidi.....	℥ii (8.0 gm.)
	Adipis.....	℥i (30.0 gm.).—M.
R.	Sodii thiosulphatis.....	℥ii (8.0 gm.)
	Glycerini.....	℥xx (1.2 mls)
	Aquæ.....	f ℥ii (60.0 mls).—M.
R.	Hydrargyri chloridi corrosivi.....	gr. i-ii (0.06-0.13 gm.)
	Tincturæ benzoini.....	f ℥i (30.0 mls)

In cases showing a pronounced inflammatory reaction, especially of ringworm of the genitocrural region (*tinea cruris*), the applications should be very mild at first, and preferably preceded for a time by a soothing lotion of boric acid (saturated solution). Sodium thiosulphate ($\frac{1}{2}$ dr.—2.0 gm. to the ounce—30.0 mls) is usually the best parasiticide to employ after the sedative treatment.

Ringworm of the Scalp (*Tinea Tonsurans*).—This is the most refractory form of the disease, although it usually yields to treatment in the course of a few months. The hair should be closely cropped, the hairs of the diseased area carefully extracted, and the scalp frequently washed with soap and water. The favorite parasitocides are betanaphthol, one dram to the ounce (4.0 gm. to 30.0 gm.); sulphur, 1 to 2 drams to the ounce (4.0-8.0 gm. to 30.0 gm.); and chrysarobin, 20 to 30 grains to the ounce (1.3 to 2.0 gm. to 30.0 gm.). Betanaphthol and sulphur may often be combined with advantage, as in the following formula:

Betanaphthol	
Sulphuris præcipitati.....	āā ℥i (4.0 gm.)
Petrolati.....	℥i (30.0 gm.)

Whatever agent is used, it should be applied for several minutes, with gentle rubbing, two or three times a day. While parasitide ointments are invariably successful sooner or later, much saving of time can be effected by x-ray treatment. In skillful hands this is the method of choice.

Ringworm of the Bearded Region (Tinea Sycosis).—

With appropriate treatment this form of ringworm usually terminates favorably in the course of a few weeks. The important therapeutic measures are the extraction of the hairs in the affected areas, thorough cleansing with warm water and soap, and the application two or three times a day of an ointment of ammoniated mercury, 30 to 40 grains (2.0–2.6 gm.) to the ounce (30.0 gm.); an ointment of precipitated sulphur, 1 dram (4.0 gm.) to the ounce (30.0 gm.); or a lotion of sodium thiosulphate, 1 dram (4.0 gm.) to the ounce (30.0 mls).

SEBORRHEA

Constitutional treatment is frequently required. Disturbances of digestion, constipation, and faulty nutrition will each require appropriate measures. Systematic exercise, preferably in the open air, the free use of water between meals, and regularity in eating often aid materially in effecting a cure.

In dry seborrhea (*dandruff*) the scales should be removed with warm water and a mild soap. Frequent washing is usually necessary. Crusts may be softened with oil or with oil to which salicylic acid, 5 grains (0.3 gm.) to the ounce (30.0 gm.), has been added. The most useful local remedies are sulphur, resorcin, ammoniated mercury, and salicylic acid.

- ℞. Cerae albæ..... ℥ii (8.0 gm.)
 Petrolati liquidii..... f ℥ii (60.0 gm.)
 Sodii boratis..... gr. x (0.6 gm.)
 Sulphuris præcipitati..... ℥ii (8.0 gm.)
 Aquæ rosæ..... f ℥vii (26.0 mls).—M.

Ft. Unguentum.

Sig.—Apply at bed time for several nights and then shampoo.

- ℞ Resorcinolis..... ℥ii (8.0 gm.)
 Olei ricini..... ℥ x–xx (0.6–1.3 mls)
 Spiritus myrciæ
 Alcoholis āā f ℥ iii (90.0 mls).—M.

Sig.—Apply between the hairs by means of an eye-dropper, using gentle friction.

Ammoniated mercury may be used in an ointment containing from 20 to 30 grains (1.3–2.0 gm.) to the ounce. Salicylic acid, 10 to 20 grains (0.6–1.3 gm.) to the ounce (30.0 gm.) may often be added to the mercurial ointment with advantage. In oily seborrhea of the face a lotion of resorcin and boric acid usually acts well.

- ℞. Resorcinolis..... gr. v–x (0.3–0.6 gm.)
 Acidi borici..... ℥i (4.0 gm.)
 Alcoholis..... f ℥i (30.0 mls)
 Aquæ rosæ..... q. s. ad f ℥iv (120.0 mls).—M.

WEIGHTS AND MEASURES.

APOTHECARIES' WEIGHT.

Troy grains.		Scruples.		Drams.		Troy ounces.		Pound
gr. 20	=	℥ 1						
60	=	3	=	℥ 1				
480	=	24	=	8	=	℥ 1		
5760	=	288	=	96	=	12	=	lb 1

APOTHECARIES' (WINE) MEASURE.

Minims.		Fluidrams.		Fluidounces.		Pints.		Gallon.
℥ 60	=	℥ 1						
480	=	8	=	℥ 1				
7680	=	128	=	16	=	0 1		
61440	=	1024	=	128	=	8	=	C. 1

APPROXIMATE FLUID MEASURES.

Teaspoonful	=	℥j.	Tablespoonful	=	℥iv.
Dessertspoonful	=	℥ij.	Wineglassful	=	℥ij.
		Teacupful	=	℥iv.	

A *drop* is usually considered equivalent to a minim, but this is the case only with a drop of water under certain conditions. The size of the drop varies with the shape of the vessel from which the liquid is being dropped and with the character of the liquid. The broader and thicker the lip of the bottle the larger is the size of the drops. Again, the lighter the liquid and the greater its viscosity the larger is the size of the drops. Chloroform and bromin, being very heavy, each drop about 250 drops to the fluidram; tinctures, spirits, and fluid extracts drop from 130 to 150 drops to the fluidram; oils, except castor oil, from 105 to 140 drops to the fluidram; syrup, from 45 to 110 drops to the fluidram; and waters and solutions, from 60 to 90 drops to the fluidram.

METRIC WEIGHTS.

1 myriagram (Mg.)	=	10,000 grams.
1 kilogram (Kg.)	=	1000 grams.
1 hectogram (Hg.)	=	100 grams.
1 decagram (Dg.)	=	10 grams.
1 gram (Gm.)	=	weight of 1 cubic centimeter of water at 4° C.
1 decigram (dg.)	=	tenth part of 1 gram, or 0.1 gram.
1 centigram (Cg.)	=	hundredth part of 1 gram, or 0.01 gram.
1 milligram (mg.)	=	thousandth part of 1 gram, or 0.001 gram.

METRIC MEASURES OF CAPACITY.

1 myrialiter (Ml. 1)	=	{ 10 cubic meters, or the measure of 10 milliliters of water.
1 kiloliter (Kl. 1)	=	{ 1 cubic meter, or the measure of 1 milliliter of water.
1 hectoliter (Hl. 1)	=	{ 100 cubic decimeters, or the measure of 1 quintal of water.
1 decaliter (Dl. 1)	=	{ 10 cubic decimeters, or the measure of 1 myriagram of water.
1 liter (L.)	=	{ 1 cubic decimeter, or the measure of 1 kilogram of water.
1 deciliter (dl. or L. .1)	=	{ 100 cubic centimeters, or the measure of 1 hectogram of water.
1 centiliter (cl. or L. .01)	=	{ 10 cubic centimeters, or the measure of 1 decagram of water.
1 milliliter (ml. or L. .001)	=	{ 1 cubic centimeter (c.c.), or the measure of 1 gram of water.

RULES FOR CONVERTING DRAMS AND GRAINS INTO THEIR METRIC EQUIVALENTS.

To convert drams into grams, *multiply* the number of drams by 3.9 grams, which is the number of grams in 1 dram. To convert grains into the corresponding metric quantity, *multiply* the number of grains by .065, which is the metric equivalent of 1 grain.

RULES FOR CONVERTING METRIC QUANTITIES INTO DRAMS AND GRAINS.

To convert grams into drams, *divide* the number of grams by 3.9. To convert grams into grains, *divide* the number of grams by .065.

EQUIVALENTS OF APOTHECARIES' IN METRIC WEIGHTS.

Grain.		Gram.		Grain.		Gram.
$\frac{1}{200}$	=	.000324		$\frac{1}{2}$	=	.0324
$\frac{1}{150}$	=	.00043		1	=	.0648
$\frac{1}{100}$	=	.00064		2	=	.1296
$\frac{1}{75}$	=	.00086		5	=	.3240
$\frac{1}{50}$	=	.00129		8	=	.5184
$\frac{1}{40}$	=	.00162		10	=	.6480
$\frac{1}{30}$	=	.00324		15	=	.9720
$\frac{1}{20}$	=	.00648		20	=	1.2960
$\frac{1}{15}$	=	.0108		30	=	1.9440
$\frac{1}{10}$	=	.0162		40	=	2.5920
$\frac{1}{8}$	=	.0216		60	=	3.888

EQUIVALENTS OF APOTHECARIES' IN METRIC MEASURES.

Minims.		Cubic centimeters.		Fluidounces.		Cubic centimeters
1	=	0.061		1	=	29.57
2	=	0.123		2	=	59.14
3	=	0.185		3	=	89.00
5	=	0.308		4	=	118.29
7	=	0.431		6	=	177.42
10	=	0.616		10	=	295.73
15	=	0.924		12	=	355.00
20	=	1.23		16	=	473.17
30	=	1.84		20	=	591.50
40	=	2.46		24	=	710.00
60	=	3.7		32	=	946.35

PERCENTAGE IN SOLUTIONS.

To estimate the quantity of a drug required to make a fluidounce or pint of a solution of a given percentage, *multiply* the weight of a fluidounce or a pint of the liquid to be used as the solvent by the percentage. Thus, in an ounce of a 10 per cent. *aqueous* solution of silver nitrate there are 45.5 grains.

$455.7 \text{ grains (weight of a fluidounce of water)} \times 0.1 \text{ (percentage)} = 45.5 \text{ grains.}$

In a pint of the same solution there are 729.1 grains.

$7291 \text{ grains (weight of a pint of water)} \times 0.1 \text{ (percentage)} = 729.1.$

If a pint of a 1 : 1000, 1 : 100, or 1 : 40 solution be required, *divide* 7291 by 1000, 100, or 40, as the case may be, to determine the quantity of the drug. Thus, in a pint of corrosive sublimate solution (1 : 1000) there are 7.29 grains of the drug.

$7291 \text{ grains} \div 1000 = 7.29 \text{ grains.}$

To determine the weight of a fluidounce or pint of a liquid other than water, *multiply* 455.7 or 7291 by the specific gravity of the liquid, and the product will be the weight desired.

INDEX

NOTE.—To obviate the inconveniences attending the use of two separate indexes—an Index of Diseases and an Index of Remedies—the author has employed but one general index. The name of each disease is printed in **bold-faced type**, and under it are grouped the remedies employed in the disease.

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